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THE OBSCURE PHYSIOLOGY OF POSTSTENOTIC DILATATION: ITS RELATION TO THE DEVELOPMENT OF ANEURYSMS

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IN THE realm of rheology, the science of flow and elasticity, there exists a curious and puzzling phenomenon known as poststenotic dilatation. Many surgeons have noted it, few have provided an adequate reason for its presence or have ventured an explanation for the mechanism of its development. William S. Halsted was greatly intrigued by it, and as usual took the problem to the experimental laboratory, where a mild dilatation distal to partial ligation of the terminal aorta was observed in seven of thirty attempts in adult dogs.[1] He suggested that the "abnormal whirlpool-like play of the blood in the relatively dead pocket just below [distal to] the site of the constriction, and the lowered pulse pressure may be the chief factors concerned in the production of the dilation." But he also stated that "it is not denied that the paralysis of the vasomotor nerves, and the occlusion of the vasa vasorum may possibly play some part in the manifestation."

Although poststenotic dilatation was first observed and described in the subclavian artery beyond a congenital cervical rib, thoracic surgeons and radiologists have become increasingly familiar with its occurrence in the presence of other congenital abnormalities of the heart and large vessels. Striking is its occurrence beyond a subaortic stenosis, as illustrated by the following case:

CASE 1.—A. M., single, aged 43, was admitted to Stanford Hospital on Jan. 25, 1953, for study and possible operation upon an aneurysm of the ascending aorta.

His past medical history revealed that ever since infancy he had been told he had a bad heart, and that he had not been allowed to play with other children. He had led a fairly normal life, except that he had been turned down by the Army because of his heart. In October, 1952, he had been seized with a pain in the right chest which was thought to be pleurisy, but which promptly subsided on restricted activity. Recent to the 1953 admission, a pain in the left chest, together with some dyspnea, had again sent him to doctors for advice, and a diagnosis of aneurysm of the ascending aorta had been made. His past history revealed treatment for syphilis twenty years previously, which was said to have been con-

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genital, since his mother had died of neurosyphilis and his sister had been treated for interstitial keratitis.

Physical examination was negative except for a moderate increase in cardiac dullness, a harsh systolic murmur heard best over the right third intercostal space, and a loud aortic second sound with a soft, blowing early diastolic murmur over the left third intercostal

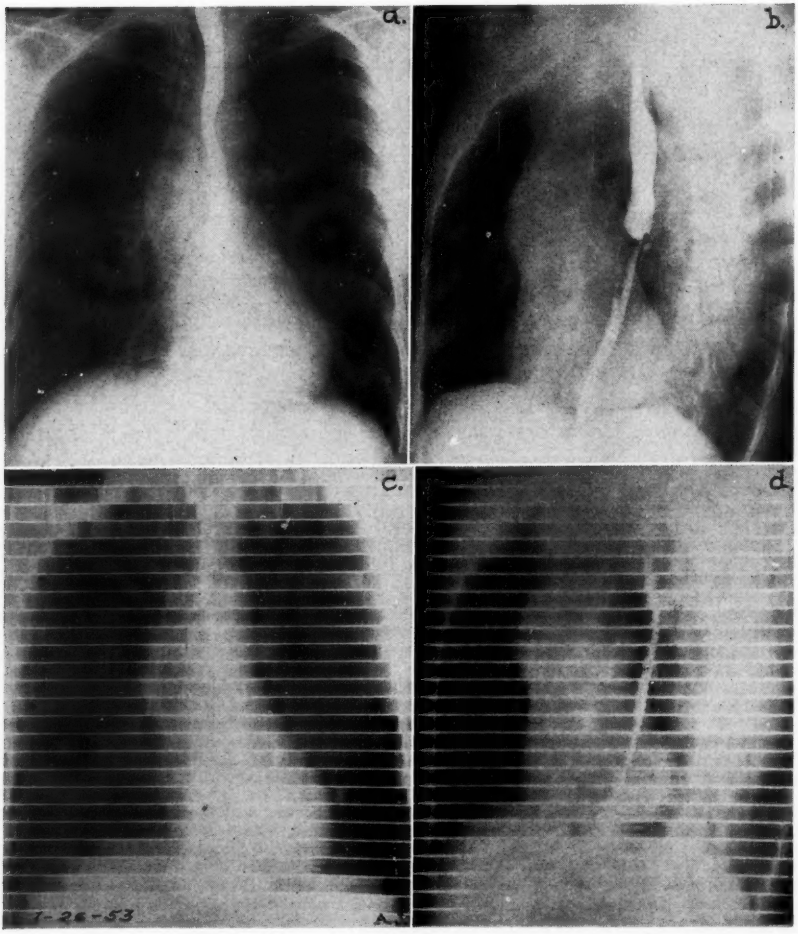


Fig. 1.—Case 1. Roentgenograms and kymograms show a markedly dilated ascending aorta originally considered a syphilitic aneurysm. However, the patient was 43 years old and was known to have had a faulty heart since infancy. A diagnosis of congenital subaortic stenosis with poststenotic dilatation was made.

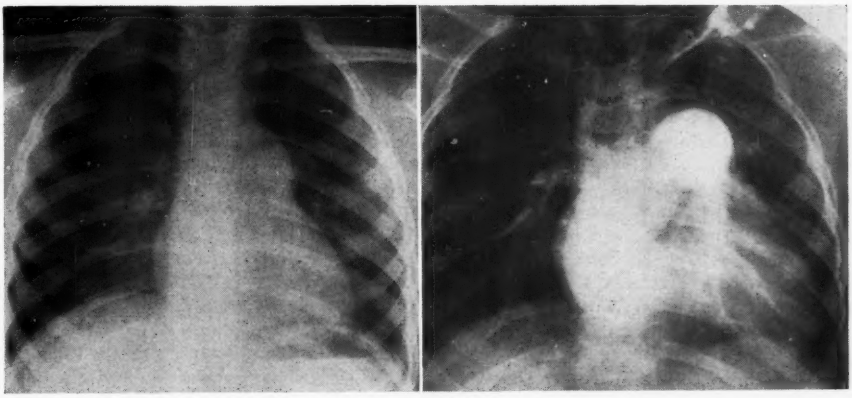
space. The blood pressure was 135/90, pulse rate 88. Roentgenograms and kymograms (Fig. 1) showed uniform dilatation of the ascending aorta with normal pulsation and with no evidence of regurgitation. Spinal fluid studies revealed a negative Hinton and a nor-

mal colloidal gold curve. The electrocardiogram was normal. A diagnosis of congenital subaortic stenosis with poststenotic dilatation of the ascending aorta was made. He was discharged without operation.

A conspicuous and more frequently seen form of poststenotic dilatation occurs distal to a congenital stenosis of the pulmonic valve, of which the following two cases are typical examples:

CASE 2.—J. B. was first seen in the Children's Cardiac Clinic on Aug. 1, 1951, when 4 years old, because of a cardiac murmur noted at birth.

Physical examination revealed a mild mental retardation, a loud harsh systolic murmur heard over the entire precordium, maximal over the second left intercostal space; pulse rate 88, blood pressure 112/70; hemoglobin 13 Gm. per cent; and 4,800,000 red cells. Roentgenograms and angiocardiograms in March, 1953, showed marked prominence and dilatation of the pulmonary artery (Fig. 2). Cardiac catheterization disclosed a right ventricular pressure of 98/4 mm. Hg, and a pulmonary artery pressure of 19/2 mm. Hg, with a femoral artery pressure of 96/60 mm. Hg. Oxygen analyses failed to disclose any evidence of an intracardiac shunt.



A. *B.*

Fig. 2.—Case 2. J. B. Roentgenograms and angiograms in a patient aged 6 showed marked prominence of the pulmonary artery. At operation a congenital stenosis of the pulmonary valve was found with marked poststenotic dilatation. *A*, Aug. 1, 1951; *B*, March 19, 1953.

Because of exercise intolerance (dyspnea and fatigue on running more than twenty yards) and the high right ventricular pressure, the patient was operated upon May 28, 1953. A valvular stenosis was incised and dilated with definite clinical improvement.

CASE 3.—R. W., aged 10, was first seen in June, 1949, at age 5, because of a cardiac murmur accidentally discovered two years previously. Although he seemed well at the present admission, he had begun to tire easily on exertion associated with the appearance of a circumoral blueness.

Physical examination revealed a loud systolic murmur maximal in the second left intercostal space, obscuring pulmonic second sound; pulse rate 88, blood pressure 100/70; good femoral pulses, hematocrit 46; hemoglobin 14 Gm. per cent; capillary oxygen saturation 96 per cent. Roentgenograms showed a marked enlargement of the pulmonary artery, confirmed by angiograms (Fig. 3).

Cardiac catheterization in April, 1951, disclosed a right ventricular pressure of 103/14 mm. Hg and a pulmonary artery pressure of 19/13 mm. Hg, with a femoral artery pressure of 125/88 mm. Hg. The catheter passed easily into the left auricle through a patent interauricular septum, but oxygen studies gave no evidence at rest of an intracar-

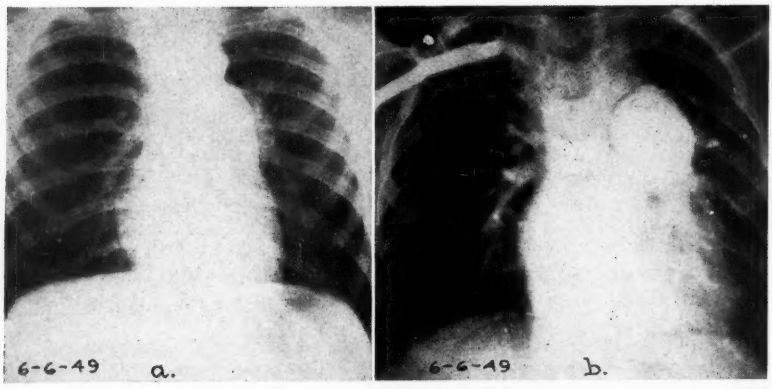


Fig. 3.—Case 3. Patient R. W. Marked prominence of pulmonary artery proved by angiograms and operation to be distal to a tight congenital stenosis of the pulmonic valve.

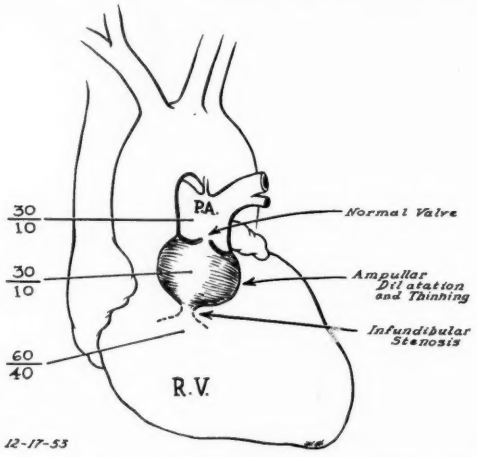


Fig. 4.—Case 4. Patient C. L. Low infundibular stenosis with normal pulmonary valve does not cause dilatation of pulmonary artery, but may cause dilatation of ampulla between the infundibulum and the valve.

diac shunt. Because of the high right ventricular pressure, operation was performed and confirmed the presence of a tight valvular stenosis with marked dilatation of the pulmonary artery distal to it.

In contrast to pulmonic valvular stenosis, the low infundibular stenosis of the pulmonary outflow tract with a normal pulmonary valve is rarely associated with dilatation of the pulmonary artery, but there may occasionally be seen in angiograms, or at operation, a small ampullar dilatation lying between the stenosis and the normal pulmonic valve (Fig. 4).

CASE 4.—C. L., a 12-year-old boy, was first seen at age 7 because of dyspnea, easy fatigability, a cardiac murmur known to have been present since birth, and a history of cyanosis at birth which soon disappeared, but which recurred slightly on exercise.

Physical examination disclosed a pale grayish cast to his skin, with questionable cyanosis of lips, pulse rate 84; blood pressure 118/82 mm. Hg in the arm, 124/77 mm. Hg in the leg; a systolic thrill in the second and third intercostal spaces with a loud systolic murmur heard over the whole precordium, but maximal in the left third intercostal space; 6,300,000 red cells, 16 Gm. of hemoglobin; and a right axis deviation in the electrocardiogram. On cardiac catheterization, a right ventricular pressure of 170/5 mm. Hg was found, with a pulmonary artery pressure of 19/2 mm. Hg and a femoral artery pressure of 110/64 mm. Hg. There was no evidence of an intracardiac shunt. Roentgenograms and angiograms (Fig. 5) showed a large right auricle and ventricle, and a small pulmonary artery, whose peripheral branches were also small.

At operation on Dec. 17, 1953, an infundibular stenosis was found, just distal to which lay a small round knob of poststenotic dilatation proximal to a normal pulmonary valve with normal pulmonary arteries. Dilatation and fragmentary removal of some cardiac muscle resulted in limited improvement.

Dilatation of the descending aorta beyond a coarctation occurs frequently, although not invariably, and may occasionally offer real difficulty in the reestablishment of continuity with the much smaller proximal aorta:

CASE 5.—C. M. was admitted to Stanford Hospital on April 4, 1952, when 3 months old because of coughing spells and difficult breathing.

At birth the baby had had a good color and weighed 7 pounds, 8 ounces. Within a few days of birth, difficult breathing accompanied by a slight but persistent cough was noted. When 23 days old, she was treated with penicillin because of a presumed bronchopneumonia. Temporary improvement was followed by gradual deterioration with increasing symptoms until readmission to the hospital.

Physical examination disclosed a poorly developed, chronically ill, pale baby, without cyanosis; pulse rate 190; respiration 74; a moderately enlarged heart, with a loud systolic murmur heard over the precordium and over the posterior lung fields; slightly palpable femoral pulses; an electrocardiogram that showed right ventricular hypertrophy; 11.7 Gm. hemoglobin; 3.75 million red cells; blood pressure 98/70 mm. Hg in the right arm, 92/60 mm. Hg in the left arm, and 58/40 mm. Hg in the left leg.

A retrograde aortogram through the left brachial artery revealed the presence of a coarctation at the usual site beyond the left subclavian artery (Fig. 6). A month after admission the child died with evidence of right upper lobe pneumonitis. Autopsy revealed a coarctation and a small interventricular septal defect.

Compression of the subclavian artery in the angle between the scalenus anticus muscle and the cervical rib to which it is abnormally attached may also produce moderate aneurysmal dilatation of the artery distal to the stenosis (Fig. 7),[2] although the astute W. W. Keen,[3] long dean of American surgeons, once expressed wonder that it did not occur proximal to the obstruction. William S. Halsted[1] abstracted 716 cases of cervical rib recorded in medical literature, and in twenty-seven cases an enlargement of the subclavian artery, fusiform, aneurysmal, or cylindrical, was described. He also reported[4] a unique example of acquired poststenotic dilatation following the application of a partially occluding metal band to the innominate artery for the cure of a subclavian aneurysm (Fig. 8). Twelve years later the common carotid artery distal to the stenosing band was strikingly dilated throughout its entire length.

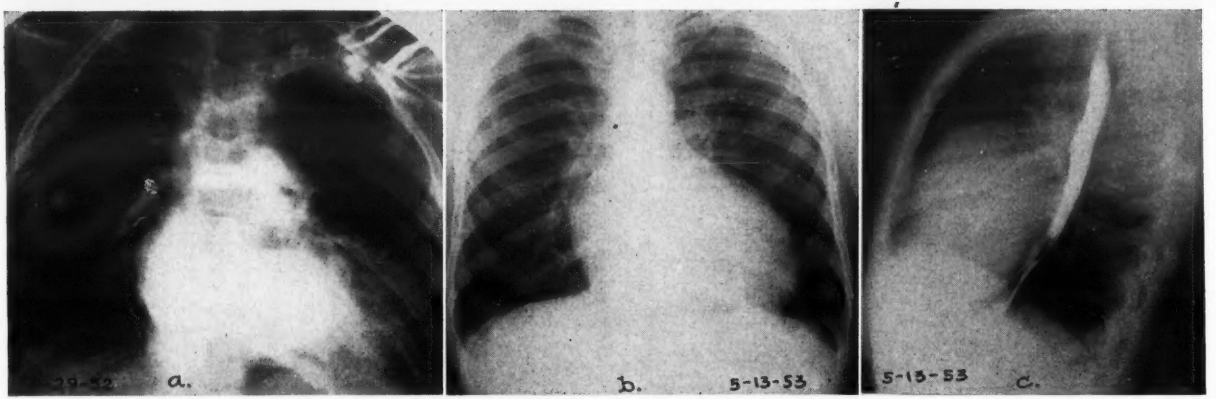


Fig. 5.—Case 4. Patient C. L. Roentgenograms and angiograms confirm absence of dilatation of pulmonary artery in presence of an isolated infundibular stenosis (see Fig. 4).

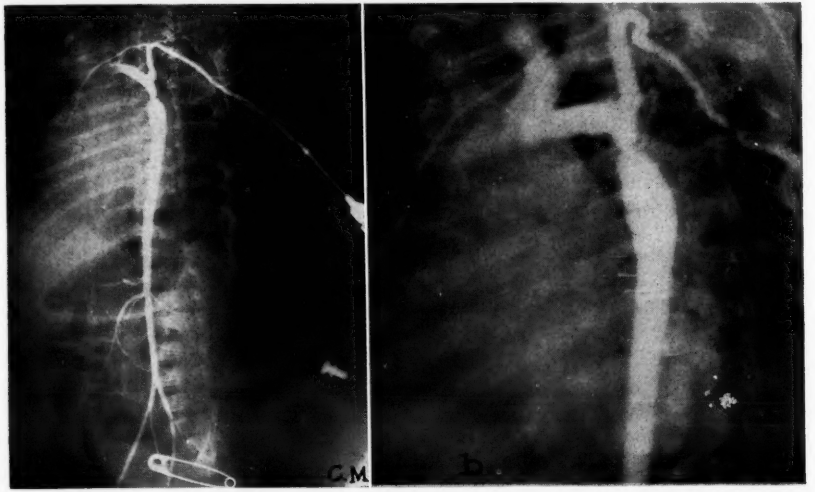


Fig. 6.—(*a*) Aortograms disclose marked dilatation of thoracic aorta beyond a coarctation in a 4-month-old infant; (*b*) dilatation in a second 4-month-old infant.

The most lucid description of the character of poststenotic dilatation as observed at necropsy is contained in a report, published in 1869, by Alfred Poland,[5] an English surgeon, who noted that "the lining membrane, as well as the middle and external coats of that portion of the artery affected by the swelling were perfectly healthy" and that "there was no atheromatous

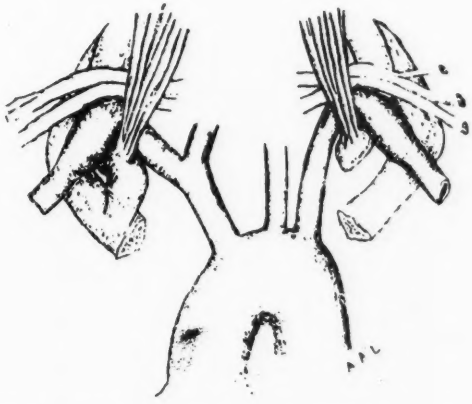


Fig. 7.—Mild bilateral aneurysmal dilatation of subclavian artery distal to compression of artery by scalenus anticus muscle at site of its attachment to congenitally abnormal cervical rib (Law: The Surgical Aspect of Cervical Ribs, Journal-Lancet 34: 330, 1914).

Fig. 8.—(*a*) Halsted's case of acquired poststenotic dilatation of right common carotid artery following partial stenosis of innominate artery by metal band for aneurysm of the subclavian artery. Aneurysm subsequently cured by ligation of subclavian artery proximal and distal to aneurysm. (*b*) During twelve years of observation, the dilatation of the carotid beyond the stenosing band gradually became more pronounced (Surg., Gynec. & Obst. 27: 547, 1918).

degeneration of the internal coat, nor any thickening of either the middle or external coats." He considered the peculiar lesion "a fusiform dilatation, unaccompanied with any special weakening of any of the three tunics, or with any rupture whatsoever. . . ."

Fig. 6.—(*a*) Aortograms disclose marked dilatation of thoracic aorta beyond a coarctation in a 4-month-old infant; (*b*) dilatation in a second 4-month-old infant.

This description of poststenotic dilatation as a fusiform enlargement without disease of the vessel wall conforms in every respect with the character of its occurrence beyond aortic and pulmonic stenoses, and beyond a coarctation of the aorta. That it can be reproduced experimentally almost at will has been demonstrated in our laboratory. Employing a technique which had previously been found effective in producing pulmonic and aortic stenosis in a study of hemicardiac hypertrophy,[6] Gerbode[7] produced coarctation of the

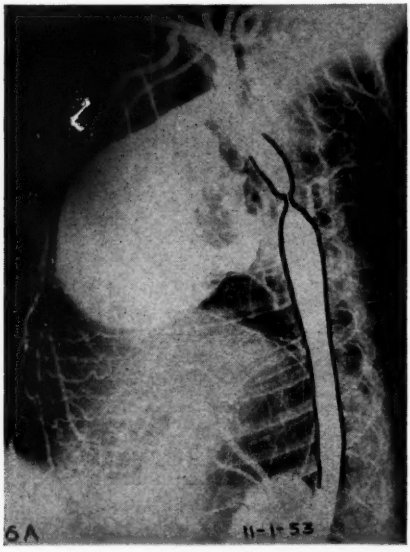


Fig. 9.—Post-mortem injection of vascular bed with 17 per cent bismuth oxychloride in a 20-month-old dog showed marked dilatation of aorta beyond an experimentally produced coarctation when pup was 8 days old.

thoracic aorta in 8-day-old puppies by a ligature so placed about the aorta that it did not constrict the lumen, but sharply limited the vessel to its primitive narrow diameter as the rest of the puppy grew to maturity. When these animals were killed one or two years later, dilatation beyond the stenosis was invariably present (Fig. 9). In our own studies, dilatation was observed eighty-four days following the application of a nonconstricting ligature to the thoracic aorta of three 21-day-old pups, all belonging to the same litter (Fig. 10).

In the course of studies to develop a method of uniting disparate cylinders,[11] the small left subclavian artery, with a diameter of 4 mm., in a 14-day-old puppy was joined to the distal end of the divided thoracic aorta, whose lumen measured 8 mm. in diameter, by the so-called V-plasty. In one instance, poststenotic dilatation immediately distal to the anastomosis appeared within twenty-four days, and in a second puppy, it was demonstrated by an aortogram at the end of ten weeks (Fig. 11). These two experiments demonstrated that

Fig. 10.—Dilatation beyond a coarcting ligature applied to the thoracic aorta was invariable, as illustrated in three pups from the same litter operated upon eighty-four days previously.

when a stream of small caliber suddenly flows into a vessel of larger diameter, the same hydraulic forces come into play as are found beyond an abrupt partial stenosis.

Experiments were then conducted with an artificial circulatory system (Fig. 12) which included a pump whose rate varied from 84 to 120 pulsations

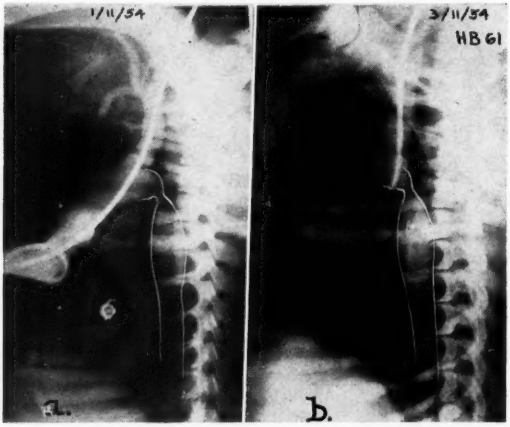


Fig. 11.—Aortograms disclosed progressive dilatation beyond end-to-end anastomosis of subclavian artery to distal end of divided thoracic aorta (*a*) ten weeks and (*b*) eighteen weeks after operation.

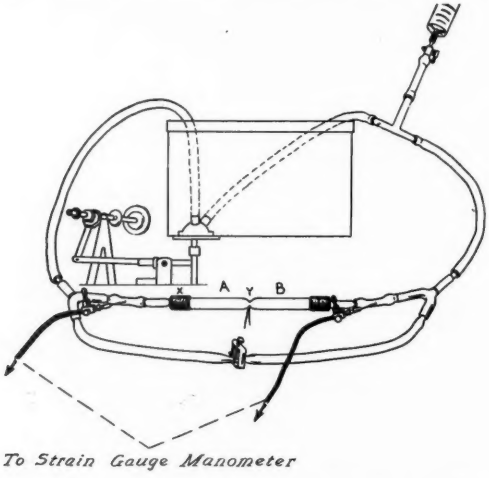


Fig. 12.—Schematic drawing of pump and conduits simulating the circulation with a segment of elastic rubber tubing introduced into system with constrictions at *X* and *Y*; capacity of system about 200 c.c. water.

per minute and whose stroke output varied from 1.7 c.c. to 9.7 c.c. The conduits consisted of rigid plastic tubing with an internal diameter of 0.6 cm., but included also a segment of elastic rubber tubing whose wall had an average

TABLE I

PRESSURE IN SYSTEM	STROKE		DIAMETER OF MAXIMUM POSTSTENOTIC DILATATION (CM.)	LENGTH OF POSTSTENOTIC DILATATION (CM.)
	RATE	OUTPUT (C.C.)		
120/70	96	5.7	2.0	1
	8 c.c. water added to system			
125/80	96	5.7	2.8	3
	Stroke output increased to 9.8 c.c.			
160/80	96	9.8	3.0	4
	Stroke output decreased to 5.7 c.c.			
125/80	96	5.7	2.5	2.5
	8 c.c. water added to system			
125/75	96	5.7	3.2	3.5
	Stroke output increased to 9.8 c.c.			
145/60	96	9.8	3.4	3.5

Capacity of circulatory system 200 c.c.

thickness of 0.033 cm. and whose internal diameter was 1.6 cm. The pressure in the system could be varied by increasing or decreasing the volume of circulating fluid, and the velocity of flow was varied by altering the stroke output. Table I records the effect upon the elastic segment of varying the pressure and the velocity of flow in the system.

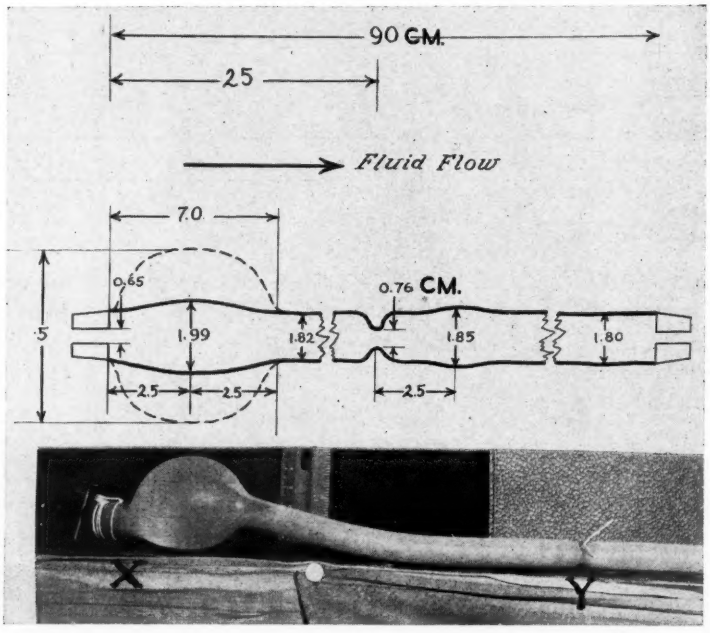
Fig. 13.—When dye is injected proximal to a constriction, remarkable eddies of turbulent and reversed flow are noted just distal to the stenosis where the rapidly ejected stream strikes the more slowly flowing and stagnant distal stream, and where high kinetic energy is transformed into high potential energy or lateral pressure.

In another experiment, the volume of circulating fluid was increased sufficiently to produce a mild poststenotic dilatation. The stroke output was then gradually reduced from 9.8 c.c. to 7.2 c.c., at which point the poststenotic dilatation disappeared. Restoring the stroke output to 9.8 c.c. caused the poststenotic dilatation to recur.

When a concentrated solution of methylene blue was injected into the lumen beyond the constriction, the dye promptly disappeared without delay into the fast-flowing distal stream. However, when the dye was injected proximal to the stenosis, there was noted just distal to the constriction a definite delay in its progress downstream (Fig. 13). It appeared to be involved in turbulent eddies before it hesitatingly resumed its forward flow. It was even seen to reverse its direction and to flow backward, momentarily, toward the stenosis. The site of delay and of turbulence of flow was identical with the site of dilatation, as well as with the location of the palpable thrill and audible bruit. Similar observations were made repeatedly.

The following experiment provided a completely convincing demonstration that the play of hydraulic forces against the elastic wall just beyond a stenosis will, in time, produce poststenotic dilatation:

A.



B.

Fig. 14.—A 90 cm. long segment of rubber tubing, 1.8 cm. in diameter, with two points of constriction was subjected to twenty-one hours of continuous pumping, at which time mild dilatation appeared beyond both constrictions. After eleven more hours of continuous pumping, during which time there was no change in the mild dilatation, the tubing suddenly ballooned out beyond the first constriction to a diameter of 5 cm. over an area about 7 cm. long. This alteration was permanent and represents maximal structural fatigue at site of greatest lateral stress.

Into the artificial circulatory system was inserted a segment of elastic tubing 90 cm. long and 1.8 cm. in diameter (Fig. 14). Twenty-five centimeters beyond the junction of the rigid tubing with the elastic tubing, a second site of stenosis was produced by partial ligation, which reduced the diameter of the tubing to about 0.75 cm. Enough water was introduced into the system to distend the elastic tubing to a normal and uniform diameter throughout, without dilatation beyond either constriction. The pump was set at 84 pulsations per minute with an output per stroke of 9.8 c.c.

After twenty-one hours of continuous pumping without the slightest evidence of dilatation, there began to appear definite but mild dilatation beyond the first constriction, with an even milder dilatation beyond the second constriction. At this time the pulsations were increased to 120

per minute. Ten more hours of continuous pumping produced no significant change in the dilatation beyond either site of constriction. Suddenly, however, after thirty-one hours of pumping and after eleven hours of mild dilatation, there occurred a remarkable aneurysmal dilatation just beyond the first constriction. An outside diameter of 2 cm. was suddenly increased to 5 cm., and the poststenotic dilatation was now 7 cm. long (Fig. 14, *B*). Moreover, the dilatation was now permanent, whether the pump worked or not. The elastic tubing had yielded suddenly and irrevocably to the play of hydraulic pressures just beyond the stenosis. Previously the mild dilatation had promptly subsided when the pumping ceased. With the appearance of the balloonlike dilatation beyond the first constriction, the dilatation beyond the second constriction disappeared completely because of the dissipation of pressure and pooling of fluid from the rest of the small system in this excessively dilated area.

In another experiment, a second 90 cm. length of rubber tubing with two points of stenosis was subjected to the continuous operation of the pump (Fig. 15, *a*). After about ninety hours of pumping, mild dilatation appeared just beyond the first constriction (Fig. 15, *b*), which subsided when the pumping ceased (Fig. 15, *c*). By applying the abrasive action of sandpaper, the wall of the tubing 2 cm. beyond the constriction was slightly thinned out, resulting in a small pouchlike dilatation at this weakened area when the pumping was resumed. The pressure in the system was then increased by the addition of only 5 c.c. of water. Instantly there occurred an accentuation of the pouchlike protrusion, followed gradually by a balloonlike dilatation of the tube just beyond the stenosis. When the pump was stopped, the aneurysmal dilatation disappeared. The effectiveness of the play of hydraulic forces in producing an aneurysmal dilatation immediately beyond a site of constriction was vividly portrayed before our almost incredulous eyes.

In another illuminating experiment, a segment of the small intestine of a cat was introduced into the circulatory system in place of the rubber tubing. After about eighteen hours of pumping, first the circular and longitudinal musculature split and then the fibrous submucosa burst 3 cm. beyond the junction of the small rigid tubing and the larger distensible intestinal lumen, the rent extending for about 2 cm.

These various observations of the effects of a stenosis in an artificial circulatory system demonstrated conclusively that poststenotic dilatation was the direct result of the play of hydraulic forces set in motion by the stenosis, and that it varied in degree with the pressure and velocity with which fluid was ejected from the stenotic channel. Moreover, there appeared to be a critical level of pressure and of velocity below which poststenotic dilatation did not occur. The element of time was most important, dilatation appearing in one experiment only after the play of hydraulic forces had persisted for a prolonged period, thirty-one hours in one experiment and ninety hours in a second experiment. It is quite evident that other important factors may determine the duration of the play of hydraulic stresses and strains necessary before dilatation occurs. These are the inherent resistance of the vessel wall to

dilatation, depending upon its structural qualities, the relationship between the elasticity of the wall and the pressure and velocity of flow to which it is subjected, the degree of stenosis present, and perhaps the viscosity of the circulating fluid. It appears that unless the stenosis reduces the lumen to one-third or one-fourth its original diameter, turbulence of flow will be minimal and only minor dilatation will occur, and may be long delayed.

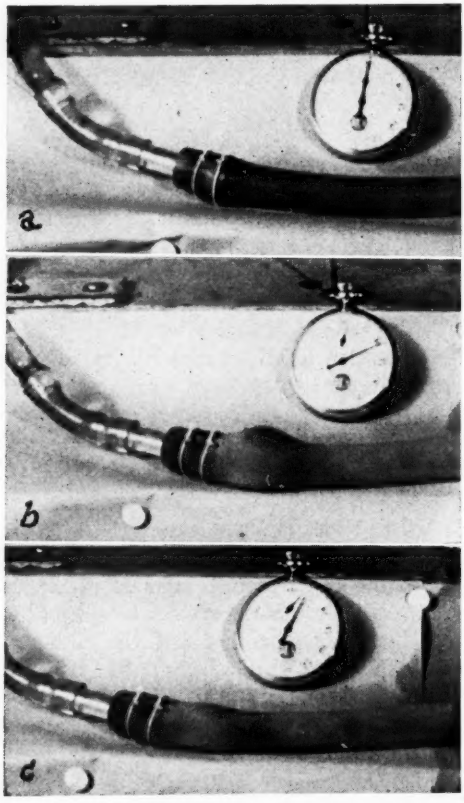


Fig. 15.—(*a*) Appearance of rubber tubing at beginning of experiment showing complete absence of dilatation beyond constriction despite pumping action.

(*b*) Postconstriction dilatation appeared after ninety hours of continuous pumping.

(*c*) Dilatation disappears promptly but not completely when pumping ceases. Incomplete disappearance due to permanent alteration as the result of structural fatigue.

In reviewing these experimental observations with due regard to certain principles of hydraulics, as emphasized by Professor John K. Vennard[8] of the Department of Civil Engineering at Stanford University, certain causes and effects were postulated as operating beyond a narrow stenosis in a large vessel transporting blood under relatively high pressure and high velocity:

During diastole in a pulsating system, there occurs normally a momentary retardation in flow which is markedly accentuated just beyond a stenosis. During systole, there emerges from the narrow stenotic channel a stream of blood at a greatly increased velocity, as compared with the velocity in the broader channel either proximal or distal to the stenosis. Mathematically, the velocity of flow, other factors remaining the same, is inversely proportional to the square of the radius. Obviously, if a tube 18 mm. in diameter is suddenly reduced to a diameter of 6 mm., the velocity through the constriction is increased nine times. Conversely, if a tube 6 mm. in diameter is suddenly increased to a diameter of 18 mm., the velocity will be reduced to one-ninth its previous rate. The rapidly ejected stream runs head on, as it were, into the more slowly flowing, and relatively stagnant, poststenotic stream, resulting in a sudden retardation in its forward flow. High kinetic energy is suddenly converted into high potential energy or lateral pressure. Moreover, the sudden arrest of the rapid stream produces eddies of turbulent and reversed flow, which strike the elastic vessel wall with alternating high- and low-pressure waves, causing the wall to vibrate, these vibrations being recognizable as a palpable thrill and an audible bruit. The location of maximal clash of streams and of the site of conversion of high kinetic energy into high lateral pressure, and therefore also the zone of greatest turbulence, lies about 1 to 3 cm. beyond the constriction, depending upon the caliber of the conduit, and upon the pressure and velocity of flow. At this point, also, the maximal dilatation occurs.

A factor supremely important to the hydraulic expert concerns the phenomenon of structural fatigue. Unevenly distributed in the zone of turbulent flow are impacts or shocks of increased pressure alternating with decreased pressure, which produce points or minute areas of high local stress against the limiting vessel wall. Depending upon the pressure in the system, the velocity of flow, and the structural qualities of the vessel wall, this oscillation of high and low pressures against the individual fibers of the vessel wall results in the prompt, or very gradual, onset of structural fatigue and in a potential thinning or distention of the wall at these points of impact. As these points of shock or stress vary in position from moment to moment and are diffusely distributed in diminishing vigor throughout the zone of increased lateral pressure, the sites of structural fatigue are correspondingly diffusely distributed in diminishing severity, resulting in a tapering dilatation of the vessel wall.

The absence of dilatation proximal to the constriction is dependent upon the concept that the pressures are evenly and uniformly distributed against the limiting vessel wall, and since the forward flow here is not subjected to sudden retardation or arrest, there is no conversion of kinetic energy into lateral pressure. General pressure proximal to the stenosis may be higher than the pressure distal to it, but it is a relatively uniform level of pulsatile pressure, evenly distributed throughout and not subject to the rapidly oscillating variations in localized pressure such as occur in the turbulent flow produced by the

clash of streams distal to the stenosis. As a result of this uniform distribution of pressure proximal to the stenosis, uniform expansion of the vessel occurs with each pulsation.

In analyzing further the play of hydraulic forces distal to a stenosis, it appears that there are three factors operating here to produce greater dilatation of the vessel: The first factor is the sudden conversion of high kinetic energy into high potential energy or lateral stress. The second factor is the turbulence of flow due to a clash of streams of differing velocities, which causes eddies of alternating high and low pressures to strike against the elastic wall. The third factor is the lowered velocity due to the widening of the stream diameter produced by the first two factors. According to the Bernoulli principle, this lowered velocity will of itself increase lateral pressure. In a pulsating stream, the first two factors recur repeatedly with each systole and set the stage, as it were, for the third factor to act, also in repetitive manner. The result of these three inexorably recurring influences in a pulsating stream, operating in a localized segment of an elastic distensible vessel, is a vicious circle: greater lateral pressure → greater widening of the stream-diameter → lessened velocity of flow → greater lateral pressure → greater widening of the stream diameter → lessened velocity of flow, and so forth. Insidiously progressive dilatation is an inevitable result unless the resistance to further dilatation inherent in the intact vessel wall itself or the incompressibility of the surrounding structures prevent it. Even these conditions may not prevent it, so effective and insistent are these hydraulic forces, given sufficient time.

Certain clinical observations confirm the great importance of the height of pressure and velocity of flow in the development of poststenotic dilatation (Fig. 16). It occurs most prominently in the ascending aorta beyond a subaortic stenosis where the left ventricle ejects blood under maximal pressure, at maximal velocity, in maximal mass, against a maximal peripheral resistance. It is almost equally prominent beyond a stenosis of the pulmonic valve where the hypertrophied right ventricle ejects an equally large mass of blood under high pressure and at high velocity. It is less prominent beyond a coarctation of the aorta since the pulsatile end pressure here is less than in the ascending aorta, the distal peripheral resistance is less, and the mass of blood forced through the coarctation and the resulting velocity of its flow have been reduced significantly by the escape of blood through the large branches of the aortic arch. Its moderate development in the subclavian artery beyond a cervical rib is also related to the lower pressure in this smaller vessel with lessened peripheral resistance beyond it. Its apparent absence beyond constrictions in vessels of still smaller caliber is related to the lower pressure and lower velocity as one approaches the periphery, where the disparity between systolic and diastolic pressures is gradually being reduced and where pulsatile flow gradually changes to more uniform and even flow. Such observations indicate that the occurrence and degree of dilatation depend upon the height of systolic pressure with which blood is thrust against the constriction, which in turn determines the velocity of flow with which blood is ejected from the short stenotic channel. The greater this velocity, the more distantly distributed

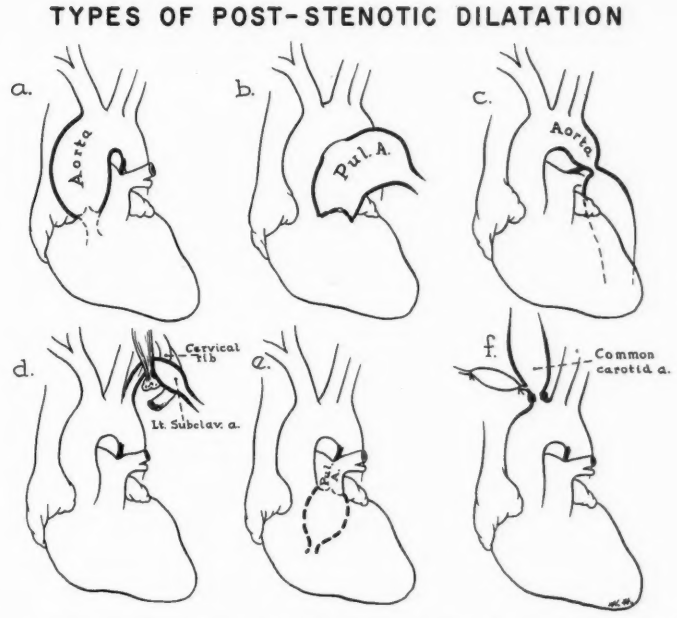


Fig. 16.—Poststenotic dilatation is most pronounced beyond a subaortic stenosis, equally prominent beyond a pulmonic stenosis, less developed beyond a coarctation of the aorta, mildly present distal to compression of the subclavian artery between the scalenus anticus muscle and its attachment to a cervical rib, occasionally present in the small ampulla between an infundibular stenosis and the pulmonic valve, and in a unique instance it occurred distal to a partially occluding band applied to the innominate artery. The degree of poststenotic dilatation is intimately dependent upon height of pressure and upon velocity of flow.

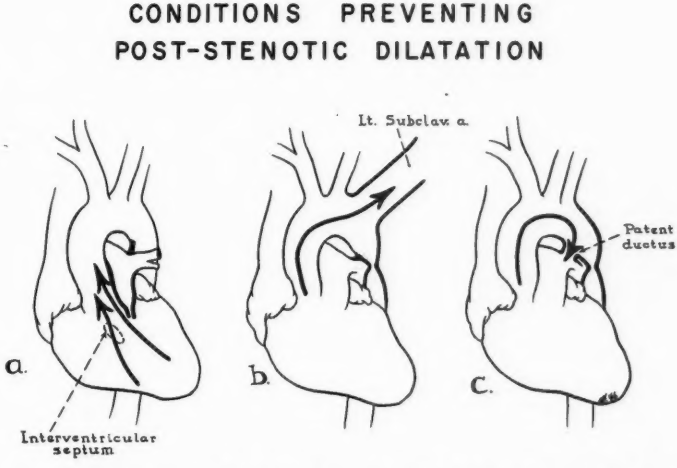


Fig. 17.—Certain conditions prevent dilatation beyond a stenosis: (*a*) an interventricular septal defect and an overriding aorta provide diversion of blood away from the pulmonary artery, thus diminishing pressure and velocity of flow through the accompanying infundibular stenosis (tetralogy of Fallot); (*b*) a large subclavian artery may divert a large volume of blood away from a coarctation, thus preventing dilatation beyond the coarctation; (*c*) a large open ductus proximal to a coarctation effectively diverts a volume of blood away from the coarctation sufficient to prevent dilatation of the aorta beyond the coarctation.

are the impacts of the swiftly flowing systolic stream against the momentarily retarded distal diastolic stream and, therefore, the more distantly effective are the shocks of increased lateral pressure against the vessel wall.

Other clinical conditions have been observed which prevent the development of poststenotic dilatation or determine its degree (Fig. 17). Most importantly, the volume of blood forced through the constricted channel and, therefore, the velocity of flow with which the blood is ejected from the stenosis may be greatly altered by conditions just proximal to the stenosis: a large collateral channel such as a greatly dilated left subclavian artery may reduce the volume flow through a coarctation; an open ductus located just proximal to a coarctation may drain a large volume of blood into the pulmonary artery away from the coarctation; an interventricular septal defect and an overriding aorta as in the tetralogy of Fallot may provide a large "runoff," or diversion, of blood away from the infundibular stenosis, thus reducing markedly the mass and the velocity of blood flow through the stenosis.

The difficulty encountered by Halsted and Reid in their experimental attempts to produce postconstriction dilatation by partial ligation of the terminal abdominal aorta may be due to the diversion of blood away from the site of partial ligation through the many large branches just proximal to it, such as the celiac axis, the two large renal arteries, the inferior mesenteric artery, and the several paired lumbar vessels. These can effectively reduce both the velocity and pressure with which blood is ejected through a stenotic channel produced in the terminal aorta and thus prevent or greatly curtail poststenotic dilatation. In our experiments, when the coarctation was produced in the thoracic aorta, where pulsatile pressure, velocity of flow, and mass of blood thrust against the constriction are higher than in the terminal aorta, dilatation beyond the coarctation invariably occurred.

That a runoff or diversion of flow away from the stenosis may effectively prevent poststenotic dilatation was convincingly demonstrated by the following case of a large patent ductus proximal to a coarctation of the aorta:

CASE 6.—K. B., aged 10,* was admitted to Stanford Hospital in January, 1954, for correction of a coarctation of the aorta accompanied by a patent ductus, both of which had been recognized soon after birth. There was no history of cyanosis.

Physical examination disclosed a very pale but well-developed normal child except for a loud continuous murmur at the left cardiac base with a loud pulmonic second sound; heart definitely enlarged and hyperactive (Fig. 18); pulse rate 98; hemoglobin 13 Gm. per cent; hematocrit 39; 4,250 white cells, urine normal; blood pressure: right arm 142/90-58 mm. Hg, left arm 140/92-60; no pressure obtainable in either leg; after the patient spent two days in bed, blood pressure in the arm dropped to 128/70-56.

At operation, a widely open ductus arteriosus, 8 mm. in diameter, was found, transmitting blood from the aorta to the pulmonary artery. Just distal to this open ductus lay a typical coarctation, but the caliber of the aorta distal to it was diminished rather than increased. The aorta proximal to the constriction had a diameter of 1.7 cm., and the distal aorta a diameter of 1.3 cm. (Fig. 19). The coarctation itself had an inner lumen of about 3 mm. in diameter. To re-establish continuity of the two disparate ends, the small distal aorta was incised longitudinally for about 7 mm. in its anterior half, thus providing

*A patient of Dr. Ann Purdy.

the necessary extra circumference for satisfactory suture to the larger proximal aorta. As a result of this V-plasty, the lumen of the anastomosis exceeded the lumen of the smaller vessel, and there was no constriction at the site of union.

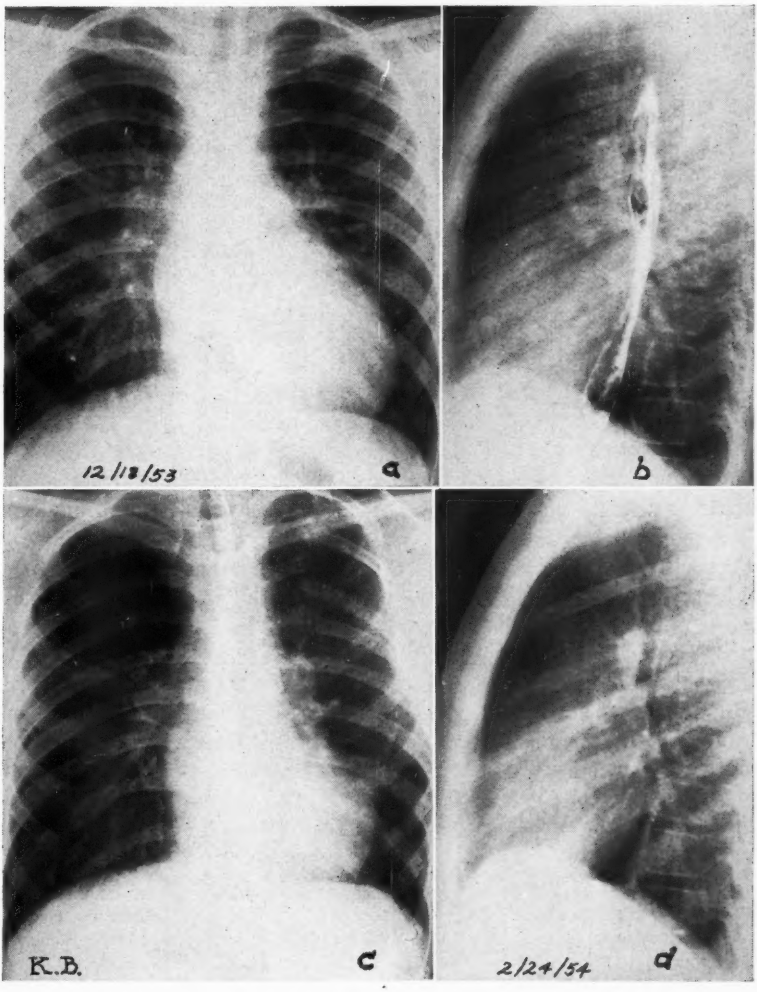


Fig. 18.—Roentgenograms (*a* and *b*) of a 10-year-old child before excision of a coarctation and ligation of a patent ductus proximal to the coarctation showed a marked dilatation of the heart which subsided promptly following operation (*c* and *d*) (see Fig. 19).

When the flow through the aorta was re-established by removing the occluding clamps, pressure in the right arm dropped from 170/110 to 120/90, and the conditions in the aorta proximal and distal to the anastomosis were promptly reversed: the proximal aorta was now smaller than the aorta distal to the anastomosis! Good pulses could now be felt in both feet, and on her discharge from the hospital ten days later, the pressure in the right arm was 128/90 and in the right leg 132/96 mm. Hg.

The absence of dilatation beyond the coarctation in this instance was the direct result of the diversion of a large volume of blood through the patent ductus into the pulmonary artery which reduced markedly the pressure and velocity of blood flow through the coarctation.

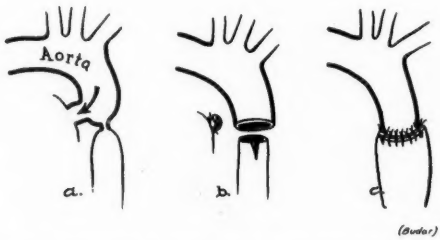


Fig. 19.—(*a*) Dilatation beyond a coarctation does not occur in the presence of a large open ductus proximal to the coarctation which diverts blood flow away from the stenosis.

(*b*) Anastomosis of disparate ends effected by use of V-plasty to avoid stenosis at site of union.

(*c*) Note larger diameter of distal aorta as compared with proximal aorta after elimination of ductus and excision of coarctation.

In the tetralogy of Fallot, in which the interventricular septal defect and the overriding aorta provide channels through which blood from the right ventricle is diverted away from the pulmonary outflow tract, no dilatation of the pulmonary artery is observed. On the contrary, in a tetralogy the caliber of the pulmonary artery and its two main branches is usually greatly diminished, commensurate with the reduced volume flow of blood through these channels. When the pulmonary artery and its branches are found to be dilated, one would suspect that the interventricular septal defect is small and that the stenosis involves the pulmonary valve rather than the infundibulum.

In the presence of pure pulmonic stenosis, without intracardiac shunts, the absence of dilatation of the pulmonary outflow tract as disclosed by roentgenograms of the chest strongly favors an infundibular stenosis. On the other hand, a dilated pulmonary artery as disclosed by roentgenograms in the presence of a presumed pure pulmonic stenosis is suggestive evidence that a valvular and not an infundibular stenosis is present (Fig. 20):

CASE 7.—W. M., aged 33, entered Stanford University Hospital in January, 1954, for possible operation upon a presumed patent ductus. He had a murmur over the heart which he believed had been present from birth, and certainly from the age of 12. He had been barred from high school football because of his heart, and had been turned down for military duty by the draft board on a cardiac disability. Recent to admission he had become more easily fatigued, associated, on excessive activity, with a dry nonproductive cough and discomfort in the chest. He disclaimed exertional dyspnea, ankle edema, cyanosis, or orthopnea.

Physical examination revealed no cyanosis, nor clubbing of the fingers, pulse rate 82, loud systolic murmur maximal in left first and second intercostal spaces, pulmonic second sound split with loud second component, blood pressure 130/74, good femoral pulses, hemoglobin 15.8 Gm. per cent, hematocrit 48, 7,100 white cells; right axis deviation, with conduction defect. Plain roentgenograms showed a marked prominence in the left hilar area which was identified by angiocardiography as dilatation of the pulmonary artery

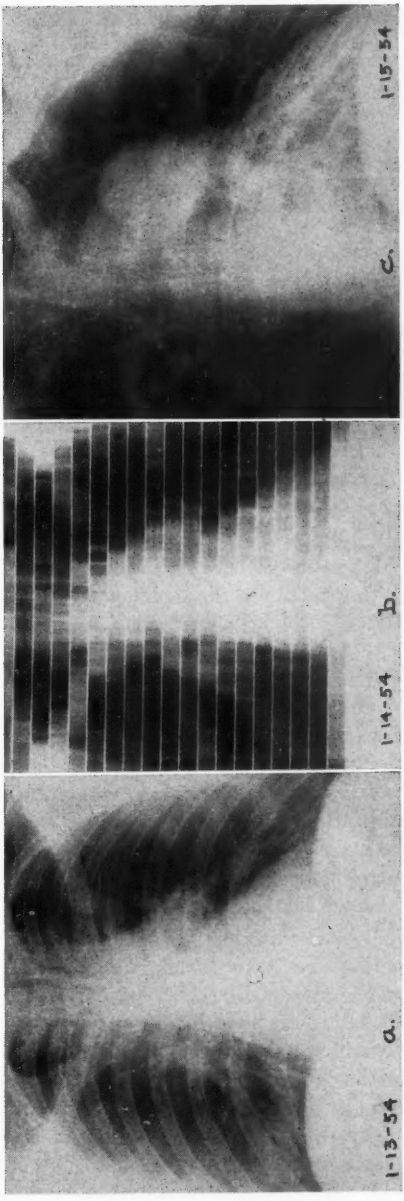


Fig. 20.—Case 7. Patient W. M. When roentgenograms in the presence of a presumed pure pulmonic stenosis without intracardiac shunts reveal marked dilatation of the pulmonary artery, it is presumptive evidence of a stenosis of the pulmonic valve rather than of the infundibulum.

(Fig. 20). A significant observation in the angiograms was the pronounced delay in the emptying of the poststenotic dilatation: dye which normally should leave this area in 3 seconds provided opacification of the dilated vessel for 4½ to 5½ seconds, a phenomenon also observed in our experimental studies of the flow distal to a constriction. Cardiac catheterization disclosed a pressure of 39/5 mm. Hg in the right ventricle, and a pressure of 19/7 mm. Hg in the pulmonary artery, and no evidence at rest of an intracardiac shunt.

A diagnosis was made of an isolated pulmonic valve stenosis without intracardiac shunt and only moderate right ventricular pressure. No immediate surgical treatment was advised, but the patient was requested to return for cardiac catheterization in one year's time to determine whether any increase in right ventricular pressure had occurred. If so, surgery would be indicated.

These experimental and clinical observations remove all doubts as to the cause of the poststenotic dilatation—it is not biologic, nor supernatural; it is not due to disruption of sympathetic nerves, nor to vasomotor paralysis; it is not the result of occlusion of the vasa vasorum nor of localized impairment of circulation; it is not the result of external trauma nor of an unusually well-developed collateral circulation entering the vessel distal to the coarctation; it is not the result of a dead pocket, nor of stagnation of fluid in this pocket. It is the simple, mechanical effect of the operation of natural hydraulic laws that govern the flow of fluid through a conduit—in this instance not a rigid-walled conduit, but an elastic vessel, capable of distention in response to increased lateral stresses repeatedly applied over a prolonged period of time.

These observations also carry other wide implications. They are strongly suggestive that the initiating factor in the development of the arteriosclerotic aneurysm may be occasionally a stenosis of the arterial lumen imposed by a segmental atherosclerosis, through which a narrowed stream flows with increased velocity into a still normally distensible distal segment, thus setting the stage for the play of hydraulic forces capable of producing a localized aneurysmal dilatation of the vessel (Fig. 21, *a*). If there is a limited area of pronounced localized weakening of the wall in the segment just beyond the stenosis, where the play of hydraulic forces is greatest, a linear rupture may occur, resulting in the initiation of a dissecting aneurysm (Fig. 20, *c*). Or a localized weakened area in the vessel wall may yield gradually to the play of hydraulic pressures, resulting in a sacculated aneurysm distal to the stenosis (Fig. 20, *b*).

Once a dilatation has been initiated, the process is perpetuated and enhanced through the application of the principle that a widened lumen slows the stream, a slowing of the stream increases lateral pressure (the Bernoulli principle), and increasing lateral pressure further dilates the vessel, thus setting up a vicious circle which is limited only by the inelasticity and rigidity of the vessel wall or by the incompressibility of surrounding structures. In reality, the play of these hydraulic forces may prove at times irresistibly destructive, as evidenced by the inexorable dilatation of an aneurysm against such seemingly incompressible or indestructible substances as bone. Through the operation of the phenomenon of structural fatigue and by the processes of compression, interference with blood supply, and consequent absorption, even the bodies of vertebrae may gradually be worn away. The progressive thin-

ning of the elastic vessel wall itself, once the dilatation has been initiated, is an additional important factor in its progressive dilatation by reducing progressively its resistance to the play of these hydraculic forces. The progressive nature of an aneurysmal dilatation once initiated is thus more easily understood.

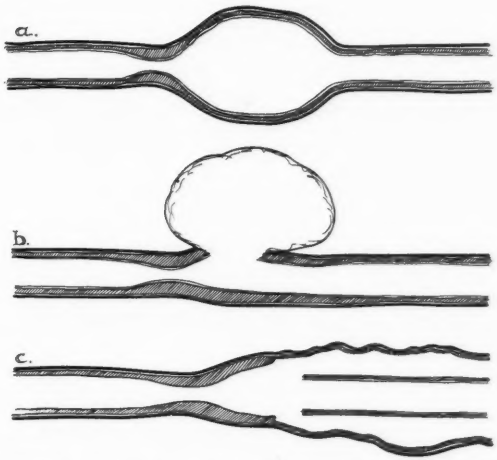


Fig. 21.—The play of hydraulic stresses accompanying the flow of blood through a stenosis due to segmental atherosclerosis in an arteriosclerotic aorta may be an important factor in the development of (*a*) a fusiform aneurysm, (*b*) a sacculated aneurysm, or (*c*) a dissecting aneurysm (see text).

Occasionally, a vessel may show segmentary thickening and rigidity of its wall due to degenerative changes without narrowing of its lumen but with complete destruction of its elasticity and with complete absence of dilatation in systole, whereas immediately distal to this rigid segment, the vessel retains its elasticity and distensibility. The emergence of a rapidly flowing stream from such a rigid segment into the more elastic and distensible distal segment may initiate a play of hydraulic forces quite comparable to those unleashed distal to a true stenosis, thus setting the stage for the development of an aneurysmal dilatation, either fusiform, saccular, or dissecting, depending upon local circumstances.

Moreover, the sudden appearance after many hours of pulsatile flow of a pouchlike dilatation or of a marked irreversible ballooning out of the rubber tubing just beyond a stenosis, as observed in several of our experiments, may well have its counterpart in the development of aortic aneurysms. A weakened area imposed by atherosclerosis or by degenerative processes in the vessel wall just beyond a stenosis may be subjected suddenly to a great increase in the play of these hydraulic forces due to the sudden increase in pulse rate and in general blood pressure accompanying unusual physical activity or great emotional strain. The suddenly heightened pressure and the increased velocity of flow through the stenosis increase greatly the hydraulic stresses localized just beyond

the stenosis, and a ballooning out of the aorta into a fusiform or a sacculated aneurysm, or even in a tear of the media with the production of a dissecting aneurysm, is the inevitable result.

SUMMARY

A mass of fluid ejected through a narrow and limited constriction under high velocity strikes against a more slowly moving mass of fluid distal to the stenosis resulting, first, in the conversion of high kinetic energy into high potential energy or lateral pressure and, second, in the lateral deflection of the rapid stream and even in a complete reversal in its direction of flow, thus resulting in a clash of opposing streams that produces eddies of alternating high and low pressures whose repeated impacts over a prolonged period against an elastic wall are capable of inducing structural fatigue and distention of that wall. Accentuating the play of these forces is a third factor: the hydraulic principle that a widening stream causes decreasing velocity which in turn produces increasing lateral pressure. The resulting interplay of these three factors recurring repetitively with each systole in a pulsating stream, and operating in a limited segment of an elastic vessel, produces eventually and inevitably the phenomenon of poststenotic dilatation. It is a highly intriguing thought that this sequence of events may be the initiating and possibly the most important factor in the development of the fusiform dilatations, the saccular aneurysms, or even of the dissecting aneurysms commonly observed in the arteriosclerotic aorta in which segmental atherosclerosis or fibrosis may produce a localized or relative stenosis.

The recognition of the potential power of the hydraulic forces liberated beyond a real or relative stenosis may assist in the explanation of the destruction of bone and surrounding structures that occasionally accompanies the development of a thoracic aneurysm. They explain also the aneurysmal dilatation of the vein usually seen at the site of an arteriovenous fistula where the arterial stream under high pressure and high velocity is ejected through an abnormal communication into the widened bed of the accompanying vein.

The occasional aneurysmal dilatation of the pulmonary artery in the presence of a patent ductus may also be ascribed to the hydraulic forces liberated when the arterial stream of high pressure and high velocity is ejected from the narrow ductus into the wider and less rapidly flowing stream of the pulmonary artery with its lower pressure.

It is highly probable, also, that the sudden cerebral hemorrhage attributed to the rupture of a small aneurysmal dilatation has its inception in the precipitate unleashing of hydraulic forces suddenly augmented by the heightened pressure and increased velocity of flow incident to emotional stress or physical exertion.

Similarly, sudden death from rupture of a larger thoracic or abdominal aneurysm may follow the sudden increase in blood pressure and pulse rate that accompanies emotional stress or physical exertion and produce an increase in neocity of flow which greatly augments the play of hydraulic forces, with result-

ing sudden increase in lateral pressure just distal to the junction of the narrow arterial lumen with the greatly widened bed of the aneurysmal dilatation.

These and other similar vascular phenomena may find their proper explanation in the application of the hydraulic laws that govern the pulsatile flow of fluid through a system of elastic vessels subjected to real or relative narrowing by congenital abnormalities, by degenerative processes, or by accidental injuries.

They give stern warning also of the need to employ, in vascular surgery, methods of end-to-end anastomosis that permit growth at the site of union as the child grows, thus avoiding future stenosis, and methods that prevent or minimize the development of constriction at the site of anastomosis, either by puckering at the time of operation, or by cicatricial contracture as healing progresses.

Grateful acknowledgment is hereby accorded to Professor J. K. Vennard of the Department of Civil Engineering at Stanford University for his helpful advice and criticism, and to Drs. Ernest Schnoor, Eldon Ellis, and Iseu da Costa, fellows in surgery, for their invaluable help in executing the experimental studies presented in this paper.

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THE ETIOLOGY OF CHRONIC INTERSTITIAL PNEUMONITIS ASSOCIATED WITH LIPID DEPOSITION

An Experimental Study

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In the last few years a form of chronic interstitial pneumonitis characterized by the presence of intracellular lipid deposition has become recognized as a pathologic entity.[1-8] Such a process may exist alone, behind bronchial obstruction or in association with other inflammatory lesions of the lung. The terms, "cholesterol pneumonia,"[4] "endogenous lipid pneumonia,"[8] and "foam cell pneumonia"[5] have been applied to this lesion to separate it from other forms of pulmonary inflammation. On the basis of the human material that has been studied, the clinical features of the disease and the pathogenesis of the lesion have been outlined in a reasonably satisfactory manner, but no specific etiologic agent has been found; in fact the slowly accumulating information on this subject indicates that the etiology is nonspecific and related to physicochemical conditions within the lung tissue of varied origin. It is surprising that this unusual and sometimes massive deposition of lipid material has not been studied more thoroughly, particularly in relation to the pathogenesis of atherosclerosis and other xanthomatous lesions.

Gross, Brown, and Hatch have reported the development of "endogenous lipid pneumonia" in rats after prolonged breathing of an atmosphere containing particulate antimony trioxide and on instillation of similar material intratracheally.[8] They suggested that accumulation of cholesterol resulted from nutritive derangement of macrophages detached from alveolar walls. Fienberg has described observations on human autopsy and surgical specimens which indicate to him that allergic phenomena affecting the bronchioles resulted in obstruction of the terminal portions of the bronchial system and that the appear-

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ance of cholesterol was secondary to obstruction.[7] Chiari[5] considered chronic lymphatic obstruction to be etiologically important, but both he and others[4] recognized certain objections to this explanation.

Our investigations have centered about attempts to reproduce this lesion in experimental animals. Bronchial obstruction by ligature or placement of foreign bodies within the bronchial lumen did not cause intrapulmonary lipid deposition in rabbits or dogs. The instillation of suspensions and emulsions of cholesterol

Fig. 1. Fig. 2.

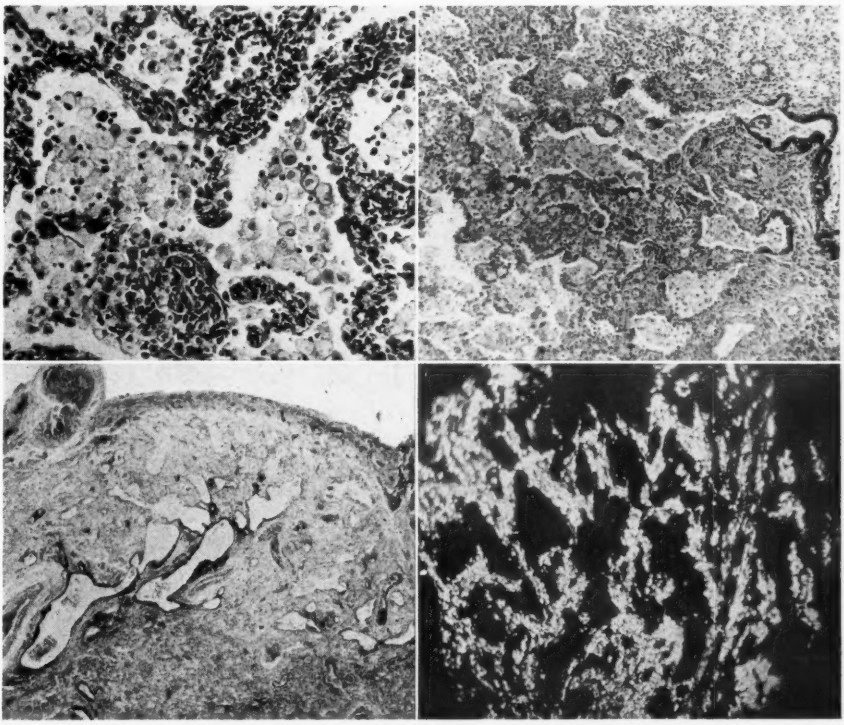

Fig. 3. Fig. 4.

Fig. 1.—The early lesion in human cholesterol pneumonitis showing lipid-filled macrophages in the interstitial tissue and air spaces. (Hematoxylin and eosin.)

Fig. 2.—A primary lobule in human cholesterol pneumonitis. The interstitial tissue is filled with lipid-containing macrophages and there is beginning fibrosis. The alveoli are obliterated leaving only alveolar ducts containing macrophages. (Hematoxylin and eosin.)

Fig. 3.—End stage of human cholesterol pneumonitis. A terminal bronchiole and branching alveolar ducts are embedded in dense collagen. (Hematoxylin and eosin.)

Fig. 4.—Doubly refractile material outlining the alveolar walls (digitonin precipitation).

into the lungs of rabbits caused inflammation and foreign body reaction which did not resemble the human lesion. X-radiation (1,600 r) of rabbits' lungs did not result in a pathologic picture that was similar to the human lesions.

Recently it has been possible to produce a form of chronic pneumonia in rabbits in which large quantities of fat and cholesterol are deposited within

activated macrophages in the lung parenchyma.[9] These experiments were carried out in two groups of rabbits. One group of animals was made lipemic by feeding cholesterol and oil. A second group of animals was maintained on stock diet. Pulmonary infections were produced in these two groups of animals by the intratracheal instillation of saline suspensions of *Pasteurella pseudotuberculosis* and a strain of *Klebsiella pneumoniae* isolated from a fatal case of pneumonia. The animals were sacrificed or died at intervals from four hours to forty-seven days. The lesions that resulted from these infections were observed grossly and studied histologically, after section and staining with hematoxylin and eosin and Sudan IV. The cholesterol-fed animals had serum cholesterol levels ranging between 1,500 and 3,400 mg. per 100 ml. of serum at the time the infections were produced.

Further observations upon the deposition of lipid in inflammatory tissues were made by ligating the major blood supply to the tibialis anticus muscles in normocholesterolemic and in hypercholesterolemic animals.

RESULTS

I. Gross Observations.—In nonlipemic animals *K. pneumoniae* or *Past. pseudotuberculosis* usually caused only small focal areas of pneumonitis some of which were identifiable only on microscopic examination. However, two animals infected with *Past. pseudotuberculosis* died within forty-eight hours of acute hemorrhagic edema without cellular exudation. The minimal lesions in normocholesterolemic (stock-fed) animals contrasted sharply with the large areas of consolidation that developed in the lungs of lipemic, hypercholesterolemic (cholesterol-fed) animals. Grossly the consolidated areas were whitish-yellow and varied from lobular distribution to massive solidification of almost the entire lung. The involved areas were airless and there was no expressable exudate. The intervening parenchyma appeared normal.

II. Microscopic Observations.—

A. Hypercholesterolemic animals: 1. Friedländer's bacilli injected intratracheally caused an initial diffuse acute pneumonitis followed by an interstitial reaction characterized primarily by large numbers of macrophages in the alveolar walls and alveolar epithelialization with apparent desquamation of the septal cells into the air spaces. Large quantities of lipid were found in all these cells regardless of their position within the lung parenchyma (Fig. 8). Cholesterol and fat were present in activated septal cells still attached to the alveolar walls, in macrophages within alveolar walls, and in free-lying macrophages in the alveolar spaces.

2. In the lungs of animals with hypercholesterolemia, *Past. pseudotuberculosis* produced an acute pneumonitis with large areas of necrosis. The surrounding zone of reaction contained many macrophages filled with lipid granules. In this zone the swollen septal cells contained lipid granules: sudanophilic material was also present in the endothelial cells of the capillaries and pleural mesothelial cells.

B. Normocholesterolemic animals: Friedländer's bacillil introduced into the lungs of rabbits on stock diet produced a focal acute pneumonitis in the first

Fig. 5.

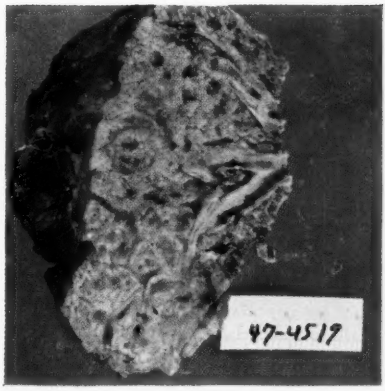

Fig. 6

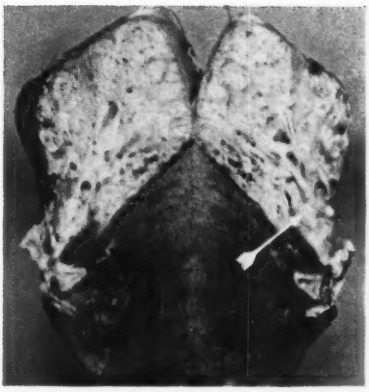

Fig. 7.

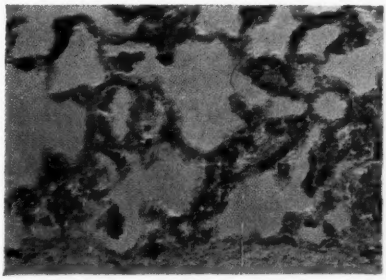

Fig. 8.

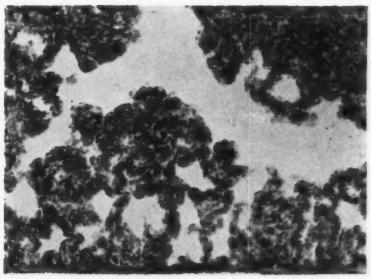

Fig. 9.

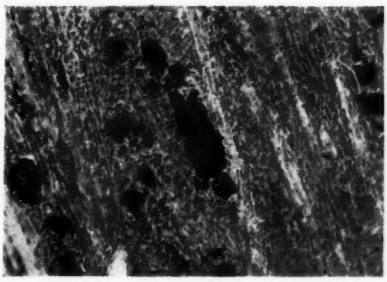

Fig. 10.

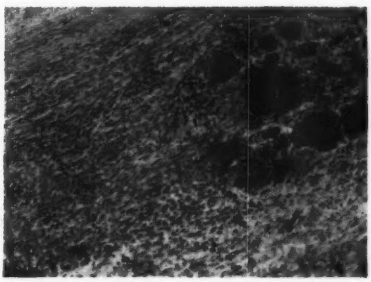

Fig. 5.—Cut section of right middle lobectomy specimen showing complete consolidation by cholesterol pneumonitis. The bronchi are freely patent.

Fig. 6.—Cholesterol pneumonitis distal to a stenosing bronchial carcinoma (arrow).

Fig. 7.—Fat stain in human cholesterol pneumonitis showing lipid-filled macrophages in the alveolar walls. (Sudan IV and hematoxylin.)

Fig. 8.—Fat stain of an area of pneumonitis in a hyperlipemic rabbit infection with *K. pneumoniae*. Lipid-filled macrophages lie in the interstitial tissue. (Sudan IV and hematoxylin.)

Fig. 9.—Lipid accumulation in the reacting cells of ischemic muscle of a lipemic rabbit. (Sudan IV and hematoxlin.)

Fig. 10.—Minimal lipid accumulation in the reacting cells of ischemic muscle of a stock-fed rabbit. Compare with Fig. 9. (Sudan IV and hematoxylin.)

few hours and subsequently an interstitial pneumonitis without tissue destruction. The exudate consisted of lymphocytes, neutrophils, and eosinophils, and, in particular, a large accumulation of macrophages in the swollen alveolar walls. There was focal migration of the macrophages into the air spaces. Fat stains demonstrated only a few lipid granules in a small number of macrophages.

C. Muscle ischemia: Ischemia in the muscles of rabbits resulted in acute necrosis of the fibers with a neutrophilic infiltration and subsequent proliferation of endomysial fibroblasts. In hypercholesterolemic animals there was a pronounced accumulation of lipid in the proliferating endomysial cells, whereas in stock-fed animals very few lipid granules had accumulated (Figs. 9 and 10).

DISCUSSION

The experimental results described herein may help to clarify some aspects of the pathogenesis and etiology of cholesterol pneumonitis in man. (1) The influence of elevated blood lipid levels upon reactions to infection has been explored. (2) The origin of the lipid material and one mechanism by which it enters the alveolar spaces seems reasonably certain. (3) There is an indication of the pathway by which fat and cholesterol may appear within macrophages. (4) Comparsion of the pulmonary reaction produced by infection in the presence of lipemia with the reaction in ischemic muscle in the presence of lipemia allows certain inferences concerning the etiology of human chronic pneumonia associated with large lipid deposits.

It is clear that under the conditions of these experiments elevated blood lipid influences the character and extent of inflammatory response in lung. In the animals infected with *Past. pseudotuberculosis,* for example, five of six lipemic animals died, whereas only two of eight nonlipemic animals died. Both of the animals in the latter group died within two days of hemorrhagic pulmonary edema. The survivors of this acute phase of the infection remained healthy and when sacrificed had normal lungs or minimal lesions. This contrasts dramatically with the extensive areas of gross consolidation that developed in the lipemic animals. The reason for this difference is not clear, but large quantities of fat and cholesterol may hamper healing and project the inflammatory reaction into a chronic phase. Cholesterol deposited in tissues is removed with difficulty[10] and its presence could account for the persistence and extension of inflammation. However, the influence of lipid deposition upon bacterial virulence and defense mechanisms remains to be explored. For example, it is possible that the function of macrophages may be impaired by a large quantity of lipid in the cytoplasm.

The lipid that accumulates within the macrophages appears to originate from the blood stream. This is indicated by the fact that in lipemic animals the edema fluid that floods the alveoli in the early stages of Friedländer's pneumonia (animals sacrificed four hours after infection) is filled with minute sudanophilic droplets. These droplets are larger than the chylomicrons of the blood and probably have coalesced to some degree. Süllman and Verzár[11] have shown that some fats permeate collodion membranes to about the same extent as proteins and lipids have been demonstrated to pass from blood into lymph.[12, 13]

It is logical that the influx of fat and cholesterol occurs from the blood stream through a damaged capillary bed in the same manner as other colloidal substances have been shown to enter inflammatory sites.[14-16]

In these experiments activated septal cells, and macrophages lying free in the alveolar space and in the alveolar walls were noted to be heavily laden with lipid material. Furthermore, in some areas of infection capillary endothelial cells were filled with fat droplets. This indicates that factors other than the mere presence of lipid within the alveoli are also of importance. Consequently the suggestion by Gross, Brown, and Hatch that lipids accumulate in intra-alveolar macrophages because of nutritive derangement seems unlikely. However, lipids released into the tissues by disintegration of the phagocytes may result in the continuation of the inflammatory response.

In hypercholesterolemic animals the accumulation of fat and cholesterol in phagocytes mobilized to clear away devitalized muscle is pertinent to experimental lung infection in the presence of lipemia. Bacterial infection was not present in the muscle indicating that it is not a prerequisite to rapid intracellular lipid accumulation. The environment in ischemic muscle and infected lung may be similar, namely, cellular breakdown products, local acidosis, activated macrophages, damaged capillaries, and lipemia. It is concluded that the physicochemical environment is of prime importance, and that the human lesion is not specifically related to any particular etiologic agent.

There is no evidence that hyperlipemia is necessary for the development of cholesterol pneumonitis in human beings. The few patients on whom blood lipid levels were measured have not shown an elevation of total fatty acids, phospholipid, cholesterol or cholesterol esters.[17] The fact that qualitatively similar lesions have been produced in animals on stock diet gives some assurance that the differences between stock-fed animals and cholesterol-fed animals are only quantitative.

In summary, intrapulmonary deposits of large quantities of fat and cholesterol have been observed in human beings, rabbits, and rats. Such lesions have been produced in rabbits as a result of two different bacterial infections and by the inhalation of particulate antimony trioxide in rats.[8] Muscle degeneration in the presence of lipemia resulted in the accumulation of fat and cholesterol in macrophages mobilized in the usual process of removing devitalized tissue. In the aorta several forms of trauma[18] and methionine deficiency[19] have led to atheromata in experimental animals. Pyridoxine deficiency can lead to arteriolar lesions with lipid deposition.[20] Fat and cholesterol accumulation in sites of chronic inflammation is a common occurrence. The common denominator would seem to be tissue injury resulting in a change of the local physicochemical conditions.

SOME GENERAL CONSIDERATIONS RELATIVE TO THE ABNORMAL DEPOSITION OF LIPIDS IN TISSUES

The water-insoluble lipids of the blood and tissues exist for the most part as stable protein-lipid complexes in colloidal solution or suspension. Like other

colloid systems the stability of lipid emulsions in the blood and tissues is dependent in part upon the electrostatic repulsion between individual molecules, micelles, and particles of like charge (a negative charge in the case of lipids). Many alterations, among them the hydrogen-ion concentration, can result in agglutination and coalescence of individual particles and "breaking" of the colloidal system. The properties of colloidal lipids are contributed to in part by the associated proteins. For example, the lipoprotein in which most of the serum cholesterol is found has an isoelectric point about 5.4.[21] Among the physical and chemical changes that occur in inflammatory tissue that might influence the behavior of lipids, the hydrogen-ion concentration in exudates and reacting cells seems of fundamental importance. Perhaps of equal importance is the behavior of proteins or other substances and their influence upon negatively charged "anionic" molecules, micelles, and particles.

Hydrogen-Ion Concentration in Injured Tissue.—It is known that tissue injury and infection result in local acidity. The increased hydrogen-ion concentration is the result of lactic acid accumulation during anaerobic or partially anaerobic glycolysis.[22] The pH values of most exudates fall in the range of 6 to 7.[22, 23] In injured tissues there is little data based on direct measurement, and hydrogen-ion concentration has been measured under few in vivo conditions. Indeed, the major effort of most physiologists working in this field has been to avoid the effects of injury. The most important contributions in this regard have been made by Needham and Needham,[24] Rous,[25] Gilding,[26] and Chambers and associates.[27, 28] Chambers gives a pH of 5.3 in injury and cytolysis. Cytoplasmic inclusions in amoebae were below pH 5.0 and apparently more acid than the surrounding protoplasm. The cytoplasmic inclusions were found to be responsive to changes in environmental pH, whereas the remainder of the cytoplasm and nucleus were not. These figures are at or near the isoelectric point of many tissue proteins and on the acid side of some. Rous found a pH of 3 or below in the cytoplasmic granules of phagocytes using litmus as an intracellular indicator.

The importance of hydrogen-ion concentration in regard to lipid deposition arises from the amphoteric nature of proteins, the effect of lowering the pH upon the actual and net charge exhibited by proteins, and the effect of these alterations upon the negatively charged colloidal lipids. Furthermore, even in the absence of proteins, changes in pH affect the stability of colloidal lipid, for each emulsion or colloidal solution is characterized by an isoelectric area. Shifts of pH toward the isoelectric point of a colloidal system detract from the stability of that system. Negatively charged lipid particles or molecules may be coalesced, agglutinated, or precipitated by pH changes that approach the isoelectric point. Similarly nullification of charge by other material may cause "breaking" of colloidal systems. It is believed that such phenomena are responsible in part for lipid accumulation in abnormal loci such as infected lung or ischemic muscle. A similar explanation may account in part for the localization of fat and cholesterol in the cytoplasm of macrophages.

The Reaction Between Basic Proteins and Lipids.—Some important features of the reaction between phospholipids and proteins are known.[29-31] Also the

extent and nature of the binding of other anions by proteins have been investigated.[32-36] This information has not been applied to the understanding of abnormal lipid deposition in tissues. One of the constant changes accompanying tissue injury or infection is an increased hydrogen-ion concentration which may involve individual cells, small groups of cells, or large masses of tissue. One of the effects of such an alteration may be that the local pH approaches or falls below the isoelectric point of some of the tissue proteins of the injured area. In general as the pH falls the proteins in that environment behave more like bases until at the isoelectric point the negative and positive parts of the molecules theoretically balance one another. Below the isoelectric point the positively charged loci of the molecule predominate and the molecule as a whole behaves as a positively charged base. Such basic molecules can react directly or form firm complexes with a variety of anions. In a broad sense the negatively charged lipids can be considered to behave as anions. Even such relatively large particles as chylomicrons enter into protein-lipid complexes that disrupt the colloidal system holding them in suspension. Complexes formed between basic proteins and lipids can generally be dissociated when the pH reverts to the alkaline side. This fact may have some bearing on the disposition of precipitated lipid in a healing lesion. At pH 4 to 5 protein-lipid complexes have been formed using normal blood serum, aqueous extracts of muscle, purified albumin, tryptic digests of serum and muscle. Phospholipid stabilized artificial triglyceride emulsions, the blood lipids of rabbits and human beings, and emulsions of pure phospholipids have been shown regularly to enter into combination with the variety of proteins mentioned above.[37]

Some proteins with high isoelectric points form stable complexes at all pH levels within the physiologic range. Protamine is a notable example of such a protein having an isoelectric point near 12.[38] Histones behave similarly. Small peptides of this sort appear from the disintegration of tissues of many types. The cleavage of nucleoprotein could result in the appearance of considerable quantities of material having qualities similar to protamine and histone.

It appears reasonable that the deposition of neutral fat, phospholipid, and cholesterol in areas of disintegrating tissue or areas of inflammation should be explained in part at least on the basis of pH changes and the reactions between amphoteric proteins of the involved tissues. Similar phenomena explain the localization of colloidal dyes and metals in areas of inflammation.[15] Undoubtedly degeneration of some tissues results in more striking effects than others and this may be explainable on the basis of the products resulting from injury to and disintegration of certain tissues. The elastin of arteries, the collagen of tendons, the ground substance itself are protein, and the slow liberation of breakdown products following injury of a variety of sorts may be one of the principal causes of the accumulation of lipid material in these tissues.

SUMMARY

K. pneumoniae and *Past. pseudotuberculosis* in the presence of high blood-lipid levels produced a pneumonitis in rabbits characterized by deposition of large quantities of cholesterol and fat in the inflammatory areas. The pathologic

lesions closely resembled "cholesterol," "endogenous lipid," or "foam cell" pneumonia previously described in human beings and were similar to several other types of xanthomatous lesions. In the presence of normal blood-lipid levels, fat and cholesterol also appeared in small amounts in chronically inflamed areas. Similar phenomena occurred in ischemic muscle, suggesting that the process was dependent upon local physicochemical conditions. The suggestion is made that local acidosis developing in an injured or infected tissue has an adverse effect upon the colloidal lipids. The effect of lowered pH is largely on the charge exhibited by colloidal lipids and proteins. The pathologic significance of the reaction between basic proteins, phospholipids, and negatively charged (anionic) lipids is discussed.

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DISCUSSION

DR. EDGAR W. DAVIS, Washington, D. C.—I have a feeling that this subject is of much greater importance than most of us recognize at the present. In the first place, there have been quite a few cases of lipid pneumonia reported as industrial hazards. In the second place, there is a segmental type of lipid pneumonia which presents a distinct diagnostic problem in differentiating it from bronchiogenic carcinoma or other forms of neoplastic disease. During the last twelve years we have operated upon six patients with "localized" or "segmental" lipid pneumonia which we believed preoperatively to be carcinoma. A report of these cases is being published in the JOURNAL OF THORACIC SURGERY. Of our six patients operated upon, only three had had bronchograms and in two of those the contrast media did not enter the diseased segments. Three of the patients gave a clinical history of the ingestion, over a period of many years, of large quantities of mineral oil for constipation. One patient had a long history of the use of oil nose drops and one patient was a high altitude aviator who used petroleum jelly around his nose and mouth to make his mask fit better. One other patient gave no history of the use of oil and had not had a bronchogram. Our pathologists felt that all of these presented the same microscopic appearance and the diagnosis of lipid pneumonia was made.

I should like to ask Dr. Waddell how a diagnosis of lipid pneumonia can be made preoperatively. Obviously, if the disease is a localized or a limited one, surgery is certainly in order. When the disease is diffuse and/or mottled in appearance, we should have some

way of making the diagnosis. In a few patients not operated upon, but whose x-rays and clinical history led us to make a diagnosis of lipid pneumonia, we have done bronchoscopies with bronchial washings, repeated bronchial washings by means of a bronchial catheter, sputum examinations and even aspiration biopsies of the diseased lung, but these specimens have failed to reveal the lipid elements. The one patient in our reported series who did not have a history of the use of oil and in whom a bronchogram had not been done makes me wonder whether or not it is possible for this to be the product of something that is not necessarily oil. Could this be the result of metabolism of cholesterol, etc.?

I enjoyed Dr. Waddell's presentation immensely.

DR. LEO ELOESSER, San Francisco, Calif.—I agree that this is an interesting and important subject. I wonder whether the paraffin aspiration pneumonias to which I think Dr. Davis refers are the same as those Dr. Waddell was discussing. I wonder whether Dr. Waddell could tell us whether the lipemia is the cause or the effect of the disease. There is a disease among sheep known as pseudotuberculosis, an epidemic disease which strikingly resembles, in the gross at least, the pictures which Dr. Waddell showed us today. Some of the members from the no longer wild but still woolly West probably know more about this disease than I do. If it occurs in sheep spontaneously, perhaps the sheep would be a more appropriate animal to work with than rabbits.

DR. HAROLD A. KIPP, Pittsburgh, Pa.—I rise to discuss this paper briefly in the light of reviewing some ancient history with which I am intimately acquainted. About 1919, under the direction of Dr. Oskar Klotz, a Canadian gentleman of distinction, at the University of Pittsburgh, I studied the variations in cholesterol in the blood serum in pneumonias. He had been interested in the deposition of cholesterol in the walls of blood vessels. This work was reported in the JOURNAL OF BIOLOGICAL CHEMISTRY, Volume 44, 1920.

The cholesterol content of the blood serum in pneumonias exhibits the following variations:

a. A primary hypocholesteremia, the degree of which is dependent upon the degree of lung involvement and the intensity of the infection.

b. A secondary hypercholesteremia in the period of convalescence, during and continuing for a varying period of time after the resolution of the pneumonic exudate.

c. A return to the normal cholesterol content of the serum.

The variation in the cholesterol in the blood serum in pneumonias is dependent upon the activity of the leukocytes, and being transported by them to the area of acute inflammation acts as an antitoxic substance, neutralizing the bacterial toxins and those arising from the disintegration of tissue in the process of the inflammatory reaction. It may also serve as an adjuvant in the development of antigens which initiate the process of resolution of the pneumonic exudate. The utilization of cholesterol in acute toxic infections is directly proportional to the severity of the disease. The development of empyema definitely alters the variation of cholesterol in the serum of pneumonia.

I should like also to note that the cholesterol content of the cellular portion of empyema exudates was three times as high as that of the fluid portion. This characteristically refractile substance could be shown microscopically in the macrophages of the exudate. Since these phagocytes move in and out of the blood serum, we presumed that the method of transport of this relatively insoluble cholesterol from blood to tissues was thus suggested. In the presence of chronic interstitial inflammation in the pulmonary parenchyma, the transport of cholesterol back into the blood stream would be delayed or prevented.

DR. WILLIAM R. WADDELL (Closing).—In response to Dr. Davis' inquiry, a sharp distinction must be made between this form of pneumonia associated with lipid deposition, and the well-known form of aspiration lipid pneumonia. The microscopic picture is easily recognized, principally by the fact that in the disease under discussion today, the lipid is uniformly distributed throughout the cytoplasm of macrophages and the droplets are extremely

minute. In either mineral oil, cod-liver oil, or other forms of aspiration lipid pneumonia or paraffinomas, the droplets vary greatly in size, and even at a glance the pathologist can distinguish between the two diseases.

The question was asked as to whether lipemia was the cause or the result of the disease. It certainly was not the result of the disease. The control series of animals underwent the same type of infection as the experimental animals and maintained normal blood lipids. The point we would like to make is that the lipemia influences the disease; it influences the normal course of two types of infection in rabbits simply by its presence.

I think the suggestion about study of the disease in sheep is pertinent to this problem and perhaps to the deposition of lipids in other diseases, principally those of the blood vessels, because it would offer an experimental setup that would perhaps be more to the point than a hyperlipemic rabbit. I think Dr. Kipp's work back in 1920 was very instructive and it pointed the way to a good deal more work that followed along the same lines. In fact, the measurement of lipid content of sputum was proposed at one time as a prognostic sign in following the course of pulmonary tuberculosis. It was ultimately given up because it correlated principally with the destruction of tissue, although it did have its advocates over a number of years.

I should like to thank each of the discussants.

ABSENCE OR HYPOPLASIA OF A PULMONARY ARTERY WITH ANOMALOUS SYSTEMIC ARTERIES TO THE LUNG

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THE interrelationship of the pulmonary and bronchial circulation in the lungs is of clinical and scientific importance. Pathologic and experimental data demonstrate the tendency for the bronchial component of this dual vascular system to enlarge when the pulmonary artery becomes smaller or is occluded. Similarly, congenital absence or hypoplasia of the pulmonary artery to a lung is often associated with compensatory growth of the bronchial or systemic vasculature of that lung. Such alterations in the blood vessels of the lung are frequently seen in association with those congenital cardiac lesions which have an absence or hypoplasia of the main pulmonary artery, and the enlargement of the bronchial blood flow plays an important role in the survival of some of these cardiac patients. Congenital anomalies of the pulmonary and systemic arteries to a lung may also occur unassociated with primary heart disease. Numerous instances of anomalous arteries from the systemic circulation being found in association with bronchogenic cysts, congenital bronchiectasis, and sequestration of a portion of the lung have been reported.[3, 4] Less common is the finding of a large systemic artery delivering arterialized blood to a lung which shows no evidence of gross anomalous development of the pulmonary tissue.[2, 8] Congenital absence of the right or left pulmonary artery may occur without abnormality of the bronchial tree or lobar development.[6, 10] In other instances a unilobar or hypoplastic lung without cystic or bronchiectatic lesions may be supplied by a small pulmonary artery and anomalous systemic arteries. Such congenital anomalies of the pulmonary and systemic vessels to one lung may result in certain alterations in the blood flow of that lung which sometimes produce symptoms. Moreover the vascular arrangements that occur in such lungs are of considerable scientific interest in an investigation of the dual pulmonary vascular system. The clinical and radiologic features of (1) absence of the pulmonary artery to one lung and (2) hypoplasia of one lung with anomalous systemic arteries is the subject of this paper.

A consideration of the embryology of the pulmonary artery and its relation to other vascular channels in the lung buds aids the understanding of the development of anomalous systemic arteries to the lung. The pulmonary vasculature is derived from both a ventral and a dorsal anlage which are joined together by the postbranchial pulmonary plexus.[5] The dorsal anlage arises

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from the aortic branches (Fig. 1). Normally these aortic connections largely disappear as the ventral segment of the plexus becomes a better-defined channel which ordinarily develops into the main pulmonary artery. But if the ventral connection to the pulmonary plexus should fail to develop normally, the dorsal aortic branches may persist. Then the lung in postnatal life may continue to receive branches from the aorta. Thus in the embryologic development of the

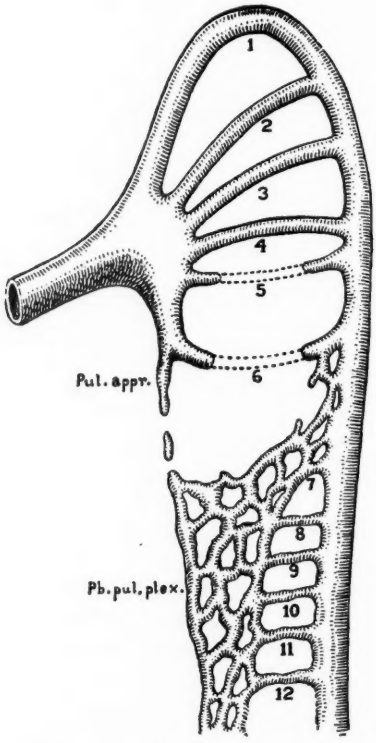


Fig. 1.—Schematic presentation of the development of the aortic arches, pulmonary plexus and pulmonary artery. *Pul, appr.*, Pulmonary artery bud. Pb. pul. plex, postbranchial pulmonary plexus. Arches 7 to 12 represent communications between aorta and the pulmonary plexus. (Reproduced from Huntington, G. S., The Morphology of the Pulmonary Artery in the Mammalia, Anat. Rec. 17: 165, 1919.)

pulmonary vasculature there is a similar tendency for the systemic or aortic components to compensate for a deficiency in the pulmonary artery channels as there is in postnatal pathologic processes. Likewise the mechanism of development of the bronchial collateral blood flow to the lungs in hypoplasia or atresia of the pulmonary artery of congenital heart disease is understandable.

It would seem logical to assume that the earlier the embryologic aberration occurs in one component of the dual vascular system of the lung, the more extensive the changes in the other component might be. It would also appear

likely that the network of vessels connecting the two vascular systems in the lung in certain congenital anomalies of the heart and lungs may be different than those produced by experimental or surgical procedures which alter the blood flow in any part of the dual system in postnatal life. Since the intrinsic intrapulmonary vascular pattern may differ in many ways depending on the exact type of vascular anomaly present, full information must await injection studies of the various types of cases.

ABSENCE OF THE PULMONARY ARTERY TO ONE LUNG

Greater use of angiocardiography has demonstrated that congenital absence of one pulmonary artery is not the extreme rarity which the literature would suggest.[12] Since some patients with this anomaly are free of significant symptoms, the condition will be definitely diagnosed only if some suggestive features of the routine chest roentgenogram are appreciated and further investigations undertaken. At present the data are too meager to justify final conclusions, but presentation of current information may aid in further evaluation. This discussion is not concerned with atresia of the main pulmonary artery in tetralogy of Fallot or other major congenital cardiac lesions.[7]

When the blood flow through one pulmonary artery is reduced or absent, either as a result of disease, surgical intervention, or congenital anomaly, the respiratory function of such a lung is largely lost. The ventilation may diminish to a varying degree. There tends to be an increase in the bronchial circulation with an increase in the functional communication between the pulmonary and bronchial vascular systems. Under conditions of marked anoxia or great carbon dioxide retention some respiratory function may be elicited in a lung which has no pulmonary artery but is supplied entirely by systemic vessels. The situation with congenital absence of one pulmonary artery may not be the same as when the main branch to one lung is occluded by disease or surgical intervention. In the case of the occluded pulmonary artery the extensive vascular channels distal to the site of obstruction may remain patent to a greater or less degree and receive blood via communications with the bronchial arterial system. Information concerning the detailed vascular arrangement within the lung in congenital absence of the pulmonary artery is lacking. Moreover the pattern will probably vary from case to case since the magnitude of the blood supply from the systemic arterial system may vary widely. Such differences in the arterial blood supply in cases of absence of the pulmonary artery may result in marked variations in the clinical and radiologic findings as well as therapeutic indications (Case 3).

Certain radiologic findings in congenital absence of a pulmonary artery permit one to suspect the diagnosis on the conventional chest roentgenogram[12] unless very large systemic vessels go to that same lung. The chief findings are (1) some reduction in the volume of the abnormal lung although the entire lung appears aerated, and (2) absence of the normal hilar vascular shadows of that lung. The diminished volume of the abnormal lung results in mediastinal displacement toward the anomalous lung and overdistention of the contralateral

lung with varying degrees of mediastinal herniation (Fig. 5). The diaphragm on the abnormal side is sometimes elevated. The degree of reduction in volume of a lung without a pulmonary artery varies considerably. In some cases the lung appears only slightly smaller than normal, whereas in other instances the reduction is considerable. This variation in lung size will naturally influence the degree of mediastinal displacement and herniation, and position of the ipsolateral leaf of the diaphragm. In some cases fluoroscopy will demonstrate mediastinal shift toward the abnormal side on deep inspiration but this finding may be absent if the lung ventilates well. The volume of a lung without a pulmonary artery may be altered by superimposed infection to which such lungs seem to be susceptible (Fig. 2). Also during life it may be difficult to ascertain definitely whether the lung has a normal number of bronchopulmonary segments unless a complete bronchographic visualization has been obtained.

Another aid in suspecting the diagnosis of absence of a pulmonary artery to one lung is to note the relative size of the hilar vascular shadows on the two sides. There will be a decrease or absence on one side with enlargement on the opposite side. The roentgen demonstration of diminished hilar vascular markings on conventional films is easier on the right than on the left side. When the pulmonary artery branch is absent on the left side, the displaced heart tends to overlie the hilar area in the posteroanterior projection.

The effect of congenital absence of a pulmonary artery branch to one lung can be considerably altered by the size and magnitude of the systemic vascular supply to that lung. Angiocardiography can give some important information about this blood flow if many films are taken in rapid succession. In cases without congenital cardiac disease the bronchial arteries, although larger than normal, are usually relatively small. If the lung without a pulmonary artery receives a very large systemic artery as in Case 3, very different clinical and radiographic findings are present (Fig. 7). The angiocardiogram usually demonstrates a fine network of bronchial vessels supplying the lung without a pulmonary artery. These vessels become opacified after the aorta has been visualized and at a time when the opaque material may have already largely cleared from the pulmonary veins of the contralateral lung (Fig. 6). This vasculature may not correspond closely in its relative distribution to the normal bronchial vascular system. In Case 2 the prominence of these bronchial vessels at the periphery of the lung is notable. If one bears in mind that the pleura in man derives its blood supply from the bronchial system, the large size of the vessels in that location is understandable. In this patient the densities cast by these collateral vessels were sufficiently prominent on the conventional film to have been incorrectly interpreted as tuberculous infiltrations.

When a lung receives no branch from the main pulmonary artery, the entire blood supply naturally comes from systemic arteries which carry arterialized blood. Although such a lung ventilates, there is no oxygen uptake from the gas in the alveoli unless the partial pressure of oxygen in the alveoli is greater than that in the arterial blood, which would only occur under abnormal circumstances. The amplitude of pulmonary ventilation noted in the lung without

a pulmonary artery has been less than that of the contralateral lung with normal pulmonary circulation. Therefore fluoroscopic examination may show deviation of the mediastinum toward the abnormal side during inspiration. This unequal ventilation may lead to an erroneous diagnosis of partial atelectasis.

In consideration of the total pulmonary function in the absence of a pulmonary artery to one lung, it must be borne in mind that a number of factors may play a role. The age of the patient, the side of the abnormality, the degree of reduction in the volume of the abnormal lung in various phases of respiration, and the extent of the bronchial and other systemic blood supply may all influence the result.

Studies of the pulmonary function in a case of congenital absence of the pulmonary artery branch to the right lung have been made by Madoff, Gaensler, and Strieder.[6] Their 14-year-old female patient showed a moderate reduction in pulmonary volumes but no evidence of emphysema. The only distinctly abnormal finding was a total ventilation which was almost twice normal because both lungs ventilated although only one absorbed oxygen. Hence there was a marked increase in the ventilation equivalent. The arterial oxygen saturation was normal.

Steinberg, Dotter, and Lukas[10] have made studies of the pulmonary function in two adults with congenital absence of a main branch of the pulmonary artery. The lung volumes, maximum breathing capacity, ventilation and blood gases were normal in a 24-year-old man with absent left pulmonary artery. In a 48-year-old woman with absent right pulmonary artery there were increased residual and total lung volumes and slight diminution of maximum breathing capacity, but intrapulmonary mixing and alveolar distribution of air were normal. Cardiac catheterization studies in the young man showed normal pulmonary artery pressure at rest with mild pulmonary arterial hypertension during exercise that doubled the cardiac output.

Because of the small number of cases of absence of the pulmonary artery which have thus far been observed, only tentative recommendations concerning therapy can be made at this time. If superimposed pulmonary infection is not present, and if the anomalous systemic circulation is not of such magnitude as to cause significant cardiocirculatory derangement, no surgical intervention seems indicated. In some cases the symptoms of chronic infection in the pulmonary tissue with abnormal circulation may indicate resection. In the rare instance in which the systemic blood flow to the anomalous lung is unusually large and results in pulmonary congestion, with or without cardiac enlargement, surgical procedures aimed at reducing, rerouting, or removing these anomalous channels must be considered. The autopsy findings in Case 3 indicated that an essentially normal distribution of the blood flow to both lungs might have resulted from a surgical transfer of the proximal end of the anomalous artery from the aorta to the side of the main pulmonary artery.

It should be noted that in our cases with symptoms of recurrent pulmonary infections there seemed to be a discrepancy between the severity and chronicity of the inflammatory process as judged from the clinical history when compared

with the gross and microscopic findings of the abnormal lung. The history seemed typical of bronchiectasis, yet repeated bronchograms showed no ectasia. Grossly and microscopically the evidence of inflammatory infiltration was meager in view of the symptomatology. Microscopically there was slight dilatation of the smaller bronchi, but the striking feature was the rather uniform thickening of the interalveolar tissues. One wonders, therefore, whether the deranged circulation played a significant role in the pulmonary symptomatology. Reliable statements concerning the walls of the blood vessels within the lung must await more extensive studies.[11]

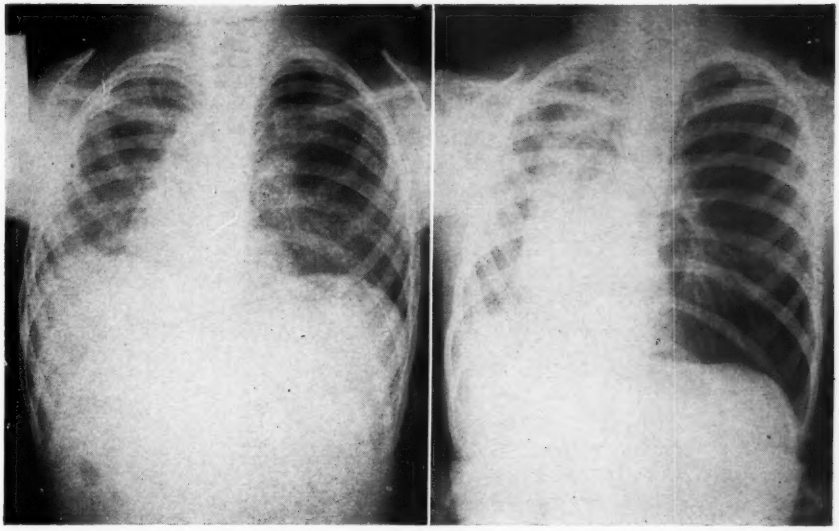
CASE 1.—A 9-year-old boy had a history of recurrent pneumonia, productive cough, and occasional hemoptysis. His respiratory symptoms dated to infancy when coughing and wheezing were noted. Bronchiectasis had been suspected for many years, but several bronchograms had been normal. Roentgenograms taken in earlier years had shown asymmetry of the thorax with narrowing of the interspaces on the right side and deviation of the mediastinum toward the right which increased with the passage of time (Fig. 2, *A* and *B*). In 1953 an anomalous blood supply to the right lung was first suspected and angiocardiograms were done. These revealed an absence of the right pulmonary artery (Fig. 3). Opacified blood was first seen to enter the right lung at the time that the aorta was visualized but no large branches to the right lung were noted (Fig. 4). Because of the history of repeated respiratory infections with productive cough and occasional hemoptysis, pneumonectomy was recommended and performed on Sept. 14, 1953. At operation there were no visceroparietal adhesions present in spite of the history suggesting repeated and long-standing pulmonary infection. The visceral pleura of the lung had a very unusual appearance in that it was a thickened layer, light gray in color, and showed numerous tiny bronchial vessels coursing over its surface. There were three lobes to the right lung with a rather well-defined interlobar fissure in the usual location. There was considerable evidence of bronchial collateral circulation in the region of the pulmonary ligament and over the lower portion of the hilum, but this was considerably less marked over the upper lobe where a 4 mm. systemic artery entered the lung at the upper border of the right upper lobe bronchus. This artery came from a systemic vessel high in the chest and descended along the trachea. This vessel had a thicker wall than a pulmonary artery of comparable size. No vessel at all was found at the place where the pulmonary artery is normally located. The entire lung was uniformly more firm than usual although no portion of it was atelectatic. The pulmonary veins were normal in their location and course and, although small, entered the pericardium in the usual location. There was no evidence of any anomalous pulmonary venous drainage. There was no enlargement of the mediastinal lymph nodes. The right lung was removed. Postoperative course was uneventful.

Microscopic examination of the excised lung revealed only slight dilatation of the smaller bronchi and very little evidence of inflammation. The striking finding was the uniform fibrosis of the lung with thickening of the interalveolar septa. This thickening was extremely uniform and not of a type usually seen with an inflammatory process.

Six months after operation the child was in good general condition but stated that he was slightly more short of breath than he had been prior to operation. It is too early to give a full evaluation of the result.

CASE 2.—A 37-year-old woman did not complain of any respiratory or cardiocirculatory symptoms until six months previously. Two years ago the first roentgenogram of the chest had been taken because the patient was a food handler. This film showed the same findings as those taken two years later. During the past six months the patient complained of a tight feeling in the right side of the chest especially in the morning and had slight shortness of breath. She had only a slight cough but recently had had some mucoid sputum.

Physical examination revealed diminished respiratory excursion of the right side of the chest. The breath sounds were considerably less prominent on the right side as com-



A. *B.*

Fig. 2.—Case 1. *A*, Roentgenogram taken at 4 years of age. Note slight mediastinal shift to the right. *B*, Roentgenogram at 9 years of age shows marked increase in mediastinal shift with elevation of the diaphragm, hyperinflation and herniation of the left lung, with decreased aeration of the right lung.

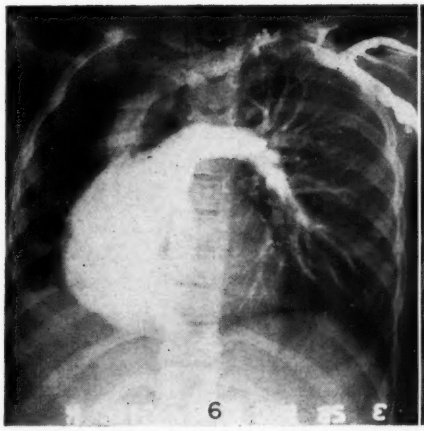


Fig. 3.

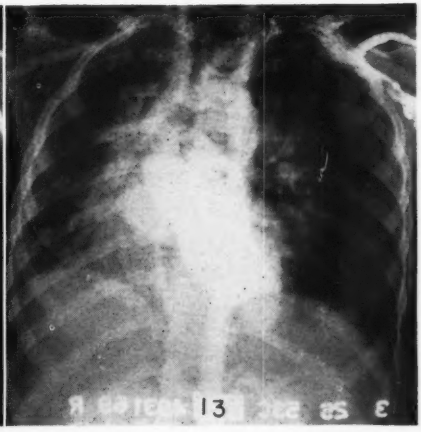
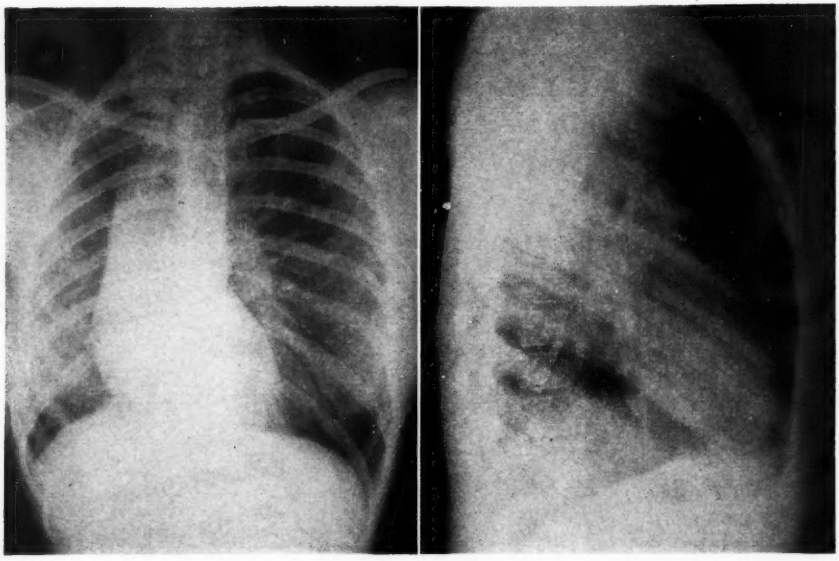


Fig. 4.

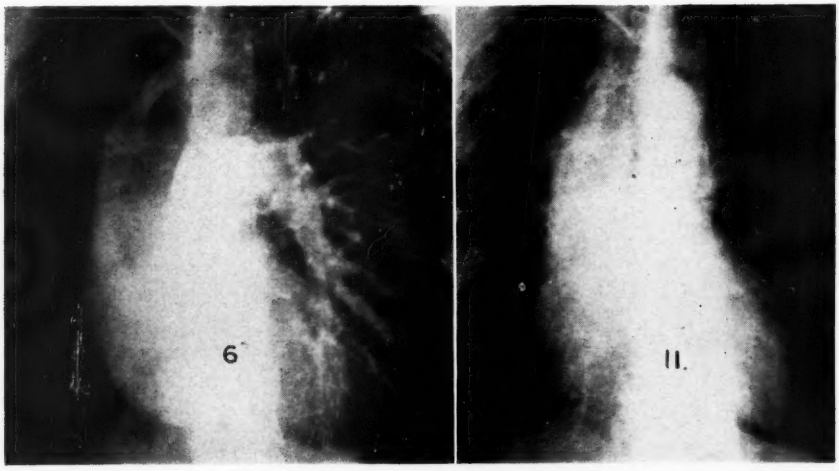
Fig. 3.—Case 1. Angiocardiogram shows a large left pulmonary artery with no evidence of a branch to the right lung.

Fig. 4.—Case 1. Angiocardiographic film taken 3½ seconds after film in Fig. 3 shows opacification of the aorta and multiple small vessels in the right lung. These tiny bronchial vessels were first opacified when the left pulmonary artery was no longer visualized.



A. *B.*

Fig. 5.—Case 2. *A*, Posteroanterior roentgenogram shows the displacement of the mediastinum toward the right side, diminished aeration of right lung, and a large left pulmonary artery. There are fine infiltration and density at the right apex. This had been erroneously interpreted as a tuberculous process. *B*, Lateral view shows the anterior mediastinal herniation.



A. *B.*

Fig. 6.—Case 2. Angiocardiogram. *A*, A large left pulmonary artery is visualized. There is no evidence of any branch to the right lung. Note the absence of any opacification in the right lung field at this time. *B*, Two and a half seconds later the aorta is opacified and a thin network of bronchial vessels is delineated on the right side. Note the opacification of the densities that had simulated parenchymal infiltration demonstrating that these shadows were produced by blood vessels.

pared to the left where they seemed to be increased. No râles were heard. The heart was displaced to the right and the second pulmonic sound was slightly accentuated. Fluoroscopy showed diminished ventilation of the right lung with some mediastinal shift to the right on inspiration and diminished excursion of the right side of the diaphragm. The left pulmonary artery seemed larger than normal. There were small linear areas of density in the right lung most marked at the periphery near the apex. These shadows had previously been erroneously interpreted as old tuberculous infiltrates. The diagnosis of congenital absence of the right pulmonary artery was suspected on the basis of the roentgenogram (Fig. 5, *A* and *B*).

Angiocardiography revealed absence of the right pulmonary artery and a large left pulmonary artery. The opacified blood did not enter the right lung until after the aorta had been opacified. The linear shadows in the right lung were demonstrated to be blood vessels which had filled from the aorta and represented hypertrophied bronchial arteries. These vessels remained opacified at the end of fifteen seconds (Fig. 6, *A* and *B*).

No specific therapy was recommended.

CASE 3.—A 4-month-old female infant was admitted to the hospital with the chief complaints of intermittent cyanosis, dyspnea, and fever. Following a normal early postnatal period, she had two episodes of cyanosis which were preceded by coughing and followed by vomiting which brought relief.

She was a well-developed and well-nourished infant. The skin was dusky gray. The respirations were rapid, and fine râles were heard at the bases of both lungs. The heart appeared to fill the entire left chest; the rate was 180 and the rhythm was regular. The heart sounds were of good quality; a systolic murmur was heard over the precordium but was heard best in the third left interspace.

Laboratory examination revealed nothing unusual. Roentgenograms of the chest showed a greatly enlarged heart (Fig. 7). The right hilar markings were more prominent than usual. There was an extensive area of increased density in the right lung field. The electrocardiogram did not show right axis deviation as would be expected in a child of this age.

Following digitalization the child was considerably improved and she was discharged with the primary diagnosis of congenital heart disease with failure. After two days of general improvement at home, the infant again showed signs of acute respiratory embarrassment as well as fever of 102° F. She was readmitted and now appeared acutely ill, dehydrated, and had gasping respirations. There were moist râles throughout both lung fields but especially at the bases. The heart sounds had not changed except that the systolic murmur had increased in intensity.

The laboratory examination showed a slight increase in the white blood cell count with a normal differential. All other special examinations failed to reveal significant information. The patient's course became progressively worse and she died eighteen hours after admission.

Autopsy Findings.—The body was that of a well-nourished, well-developed infant. The volume of the left lung was decreased by one-half because of the enlarged heart. The interlobar fissures were normal in number and location. On sectioning the lungs, scattered irregular hemorrhagic areas were noted throughout both lungs. There was frank consolidation of the right upper lobe. On microscopic study confluent lobular pneumonia was present in the upper and lower lobes of the right lung and the lower lobe of the left lung.

The greatly enlarged heart weighed 80 grams. There was equal dilatation and hypertrophy of both ventricles. Both auricles showed dilatation, but the right was twice as great as the left. Venae cavae and pulmonary veins entered the auricles at their usual sites. The coronary sinus was normal, but the foramen ovale was patent. The pulmonary valve measured 2.9 cm. and the aortic valve 2.2 cm. in diameter. The heart was otherwise normal.

The coronary arteries arose normally. One centimeter above the aortic valve a large vessel 2.7 cm. in diameter arose from the left side of the aorta. This artery crossed the mediastinum to enter the right lung.

The pulmonary artery was of normal caliber, measuring 2.5 cm. in diameter at its origin and 1.7 cm. in diameter beyond the dimple of the ligamentum. There was one branch to the left lung, but none to the right. Microscopic examination of the left pulmonary artery and the abnormal right pulmonary artery failed to show any difference in their mural structures.

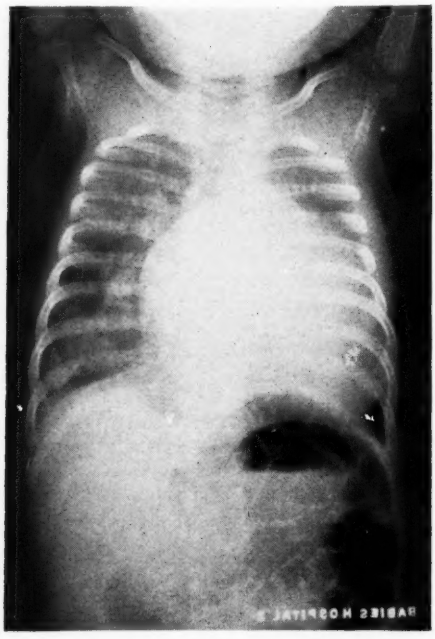
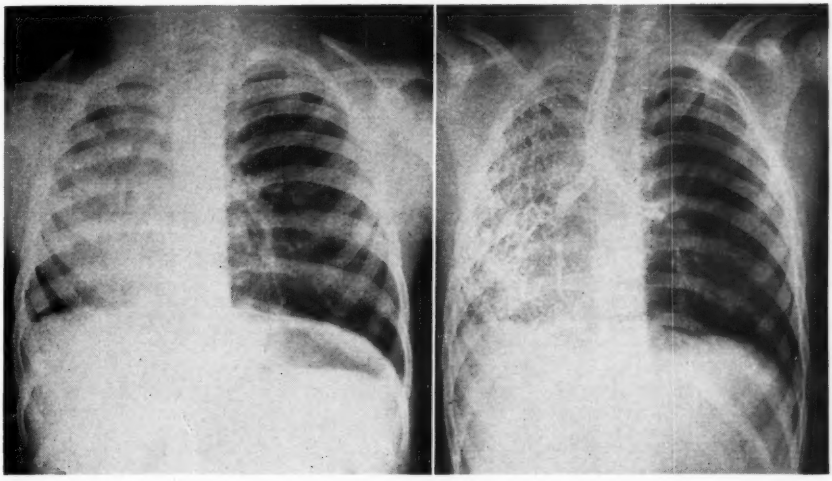


Fig. 7.—Case 3. Note the greatly enlarged heart and the increased vascular markings in the right lung.

HYPOPLASTIC LUNG WITH ANOMALOUS SYSTEMIC ARTERIES

Varying degrees of hypoplasia of a lung may occur. If the embryologic aberration is so extensive that a lung consists of less than the equivalent of a single lobe, it is unlikely that a clinically significant amount of normal respiratory tissue will be present. In the markedly hypoplastic lung congenital bronchiectasis and bronchial cyst formation usually constitute most of the maldeveloped lung. Even a unilobar lung with relatively normal pulmonary tissue is rare.[9] In an incompletely developed lung the pattern of the bronchial tree may vary widely and the single lobe in a unilobar lung may have a bronchial distribution which does not correspond to that of any normal lobe. Therefore it may be difficult to assess what the normal volume of a specific hypoplastic lung should be. The finding of emphysema and marked cardiac displacement to the involved side suggest that perhaps a small amount of pulmonary tissue has been overdistended.

CASE 4.—A 12-year-old girl complained of being short of breath on exercise such as walking upstairs and riding her bicycle. The shortness of breath was said to have definitely increased during the past year. She had no history of pulmonary infection. When six months of age a chest roentgenogram was reported to have shown diminished aeration throughout the right chest with no lung markings distinguishable. The heart shadow was reported to be very indistinct and on the right side. Several years later a bronchogram was done. An anomalous right bronchial tree without evidence of bronchiectasis was demonstrated (Fig. 8, *A* and *B*).

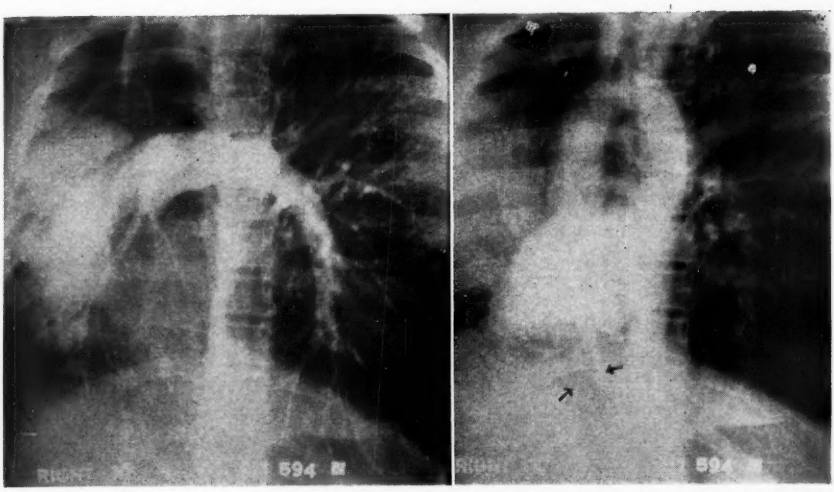


A. *B.*

Fig. 8.—Case 4. *A*, Roentgenogram at 4 years of age demonstrates dextrocardia and diminished volume of the right lung. Note the vagueness of the cardiac outline. *B*, Bronchogram several years later showed an anomalous bronchial tree on the right side without bronchiectasis.

Since this girl had apparently more normal pulmonary tissue than following pneumonectomy and yet had more shortness of breath than one would expect in a 12-year-old person after pneumonectomy, it was considered probable that the pulmonary disability was due to abnormal blood flow to some of the pulmonary tissue. Since the radiologic findings were very similar to Case 5, which had been seen several years earlier, it was considered probable that the girl had anomalous systemic arteries entering the hypoplastic right lung. An angiocardiogram was therefore recommended. This investigation was done through the courtesy of Dr. Charles Dotter. The angiogram showed marked displacement and some rotation of the heart in the right hemithorax. There was a large left pulmonary artery and a small right pulmonary artery. After the abdominal aorta had been opacified, two arterial branches were visualized coursing along the medial aspect of the cupola of the right diaphragm and apparently entering the base of the hypoplastic right lung (Fig. 9, *A* and *B*). As a result of this anomalous blood flow there was prolonged opacification of the right pulmonary vein.

Studies of respiratory function were performed through the courtesy of Dr. John West in the Cardio-pulmonary Laboratory of the Presbyterian Hospital. The vital capacity was normal. Although the residual volume was perhaps slightly increased the ratio of residual volume to total capacity remained in the normal range. Ventilatory studies showed a



A. *B.*

Fig. 9.—Case 4. Angiocardiogram. *A*, Demonstrating a large left pulmonary artery and a small branch to the right lung. The main portion of the right branch is superimposed on the left branch in this projection but some of the smaller branches can be seen going to the lower portion of the right lung. *B*, Later film with aorta opacified demonstrates two branches indicated by arrows entering the lower portion of the right lung.

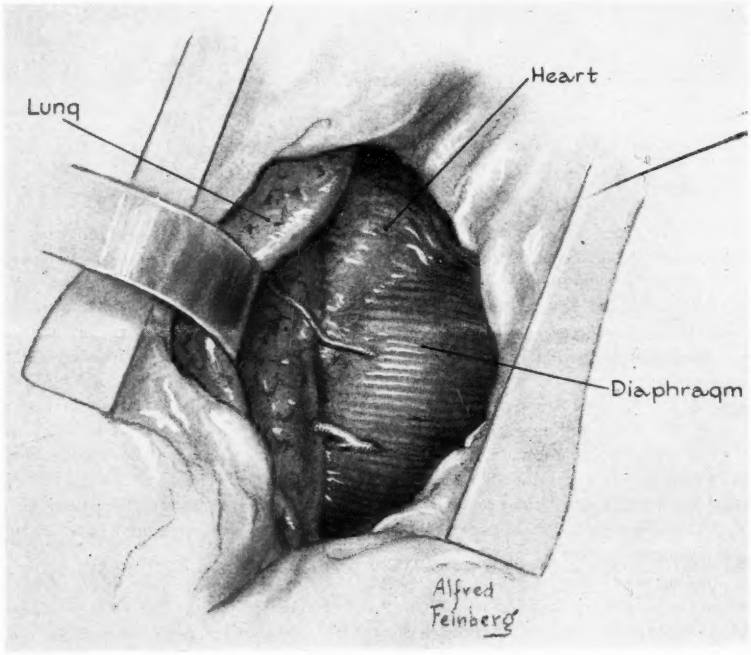


Fig. 10.—Case 4. Artist's drawing of operative finding. Note the two systemic arteries traversing the diaphragm and entering the base of the hypoplastic right lung.

slightly reduced maximum breath capacity but no evidence of obstructive breathing. Some hyperventilation was seen at rest. Studies of the gas exchange revealed normal arterial oxygen saturation and carbon dioxide tension both at rest and after exercise.

In December, 1951, the right hemithorax was explored. There was no free pleural space except over a limited area of the lower posterior and lateral thoracic wall and a part of the diaphragmatic surface. Here there was a well-defined pleural space without adhesions and the reflection of the parietal pleura onto the lung at the border of this space suggested anomalous absence of the visceral pleura elsewhere. Except for the pleural pocket mentioned, the lung was diffusely adherent to the chest wall and mediastinum by avascular connective tissue which was traversed by some small blood vessels in a plane parallel with the surface of the lung. The pulmonary tissue in general appeared normal. There was no evidence of emphysema. There was relatively little anthracotic pigment. There was a systemic artery measuring about 6 mm. in diameter perforating the dome of the diaphragm slightly posterior to the middle in an anteroposterior plane. This artery entered the undersurface of the lung and then coursed along the lung tissue just beneath the surface and continued to have the thickness and anatomical characteristics of a systemic rather than a pulmonary artery. A second systemic artery was found further posterior and somewhat more medial close to the vertebral bodies. It too came through the diaphragm, measured about 8 mm. in diameter, and divided into a small and large branch before entering the lung posteriorly in the paramediastinal portion (Fig. 10). The further course of this artery in the lung was not visualized. Both arteries which perforated the diaphragm had strong pulsations and obvious systemic arterial pressure. A small lymph node was present at the site of entrance of each artery into the lung substance.

The two arterial branches described above were dissected out, ligated and divided.

The postoperative course was uneventful. Since operation two and a half years ago the patient no longer complains of any shortness of breath and has continued to develop normally. Radiographic examination of the chest shows no change from the preoperative appearance.

CASE 5.—A 36-year-old woman had complained of dyspnea on exertion for seventeen years. When 12 years old she had migratory joint pains and fever. Even as a child she became readily short of breath. She had had occasional blood spitting during the past seventeen years, usually in the form of pinkish mucus. At one time she was admitted to a tuberculosis hospital but no tuberculosis was found. It was known that her heart was in the right side of her chest.

Physical examination revealed a thin, poorly nourished woman without cyanosis. Both sides of the chest moved equally on respiration but the heart was to the right of the midline. There was a rough systolic murmur at the base of the heart and a softer systolic murmur at the apex. The electrocardiogram did not demonstrate the findings of a true dextrocardia. Roentgenographic examination of the chest showed that the heart was displaced to the right of the midline and there was herniation of the left lung through the anterior mediastinum. The lung fields were clear and the diaphragm moved normally. There was no evidence of infiltration or atelectasis of the right lung. Bronchographic examination delineated the bronchial tree of a right upper lobe which was over expanded and extended down nearly to the diaphragm but no bronchial tree of the middle or right lower lobe was outlined. The bronchial tree of the left lung appeared normal. At bronchoscopy the carina was noted to lie obliquely so that the left main bronchus arose in an anterolateral direction and the right main bronchus rose in a posterolateral direction. The right upper lobe bronchus appeared normal, but a short distance beyond this the bronchus narrowed to such a marked degree that inspection beyond this point was not possible. It was erroneously assumed that the bronchus was occluded by a mass. Biopsy of the bronchial wall showed no tumor.

Pulmonary function studies by Dr. John West revealed a 50 per cent reduction in maximum breathing capacity and pulmonary distention evidenced by large residual air but no evidence of alveolar dysfunction. There was considerable hyperventilation at rest

with a low rate of oxygen removal at rest which rose to almost a normal level during exercise. The oxygen and carbon dioxide content of the arterial blood was normal during rest and exercise.

A thoracotomy revealed no free pleural space. The right hemithorax contained a unilobar lung. The heart occupied a considerable part of the lower and anterior portion of the right hemithorax. As the lung was freed from the diaphragm, several vessels were found penetrating the diaphragm close to the midline and entering the pulmonary tissue. Two of these were systemic arteries and one of these two arteries was ligated and divided. Both systemic arteries were not ligated and divided because it was not known at that time whether the lobe was also supplied by a pulmonary artery.

CASE 6.—A 14-year-old boy had frequent upper respiratory infections and a persistent cough which gradually became productive of one-half cup of yellowish sputum daily. Although his activities were not seriously curtailed, he was moderately dyspneic on exertion. One month prior to admission he began to complain of weakness and fatigue. He coughed up a teaspoonful of blood at this time and again two weeks later.

There was decreased expansion of the right chest with diminished breath sounds, dullness, and numerous râles on that side. A rough systolic murmur was heard in the right second and third interspaces. Roentgenogram showed a shift of the heart and mediastinum to the right, elevation of the right diaphragm, and intercostal narrowing on the right due to diminished volume of the right lung of long duration. Bronchogram showed a well-outlined bronchial tree of the right upper lobe, which was overexpanded. The right main stem bronchus ended in a blind sac.

At operation the right pleural cavity was obliterated by exceedingly dense and vascular adhesions. There were several firm bands from the diaphragmatic pleura to the lower surface of the lung containing vessels measuring 2 to 3 mm. in diameter. There were no normal pulmonary arteries or veins on this side. A large vein left the single lobe, ran parallel to the bronchus, and emptied into the superior vena cava. The hypoplastic right lung was removed.

Microscopic examination revealed diffuse emphysema with alveolar rupture throughout the lung parenchyma. The pouch representing the undeveloped main stem bronchus demonstrated all normal bronchial elements.

Two of the patients who had a hypoplastic, unilobar right lung with a small pulmonary artery and several systemic arteries going to that abnormal lung had rather similar findings (Cases 4 and 5). The older of the two had symptoms in adult life which it is hoped the younger will not develop because the anomaly was diagnosed and treated at an earlier stage. It is my impression that the systemic vessels which entered the hypoplastic but uninfected and ventilating lung resulted in an augmented blood flow with high pressure to that lung. It must be borne in mind that the situation was quite different from that which is created when a systemic artery is surgically joined to a pulmonary artery in order to increase the blood flow through the lungs in pulmonary stenosis. In the latter situation the pressure in the pulmonary artery is not greatly elevated a short distance from the anastomosis unless secondary changes in the small pulmonary vessels have occurred.[11] In contrast, however, are the findings when an anomalous systemic artery with its thicker wall conducts the blood into the pulmonary tissue. At operation it was striking to note the way the pulsation of the small artery could be readily felt out into the smaller branches of the vessel. The intravascular pressure was undoubtedly much higher than in a normal pulmonary artery. I believe it is reasonable to assume that the dyspnea which was the first and chief complaint in these two patients was due to local

pulmonary engorgement and that the patients' hyperventilation was produced by the same mechanism. The disappearance of any complaint of dyspnea in the patient who had the systemic arteries to the hypoplastic lung interrupted over two years ago supports this contention.

The two patients with a unilobar right lung, small pulmonary artery and systemic arteries arising below the diaphragm had many unique features in common. The roentgen appearance in both cases was very similar. A striking finding was the degree of mediastinal displacement which was so marked that dextroposition of the heart was present. Moreover the right heart border was not clearly outlined but merged with other shadows in the lower two-thirds of the right hemithorax (Fig. 8). The degree of cardiac displacement and rotation was much greater and dissimilar to that seen after surgical removal of the right middle and lower lobes. The small volume of the anomalous lung might be a combination of (1) being only one lobe, (2) reduced volume as a response to the abnormal systemic blood supply, and (3) pleural factors. In neither case did the visceral and parietal pleura appear normally developed throughout that hemithorax. The appearance simulated obliteration of most of the pleural space by adhesions but actually the lung tissue seemed to be attached to the chest wall by loose connective tissue. There was a distinct pleural pocket between the base of the lung and the diaphragm in one case, but this pleura seemed to be merely reflected from chest wall onto lung at the margins of this pocket and not continued as a parietal pleura lining the hemithorax. Moreover the surface of the lung did not present the usual surface markings or arrangement of bronchial vessels. Whether these atypical pleural findings contributed to the unique roentgen appearance can only be conjectured.

DISCUSSION

The blood flow from an anomalous systemic artery into a lung may be influenced by (1) size of the vessel and its branches, (2) character of the wall of the anomalous vessel, especially in regard to its muscular and elastic components, (3) pressure within the vessel and the intravascular resistance, (4) degree and type of intercommunications with the pulmonary arterial branches when the pulmonary artery is not absent, and (5) nature of the venous system in the lung. Whether the neurogenic influence on the wall of such anomalous vessels is significantly different from that of normal pulmonary vessels is a matter for speculation. Moreover there are no data concerning the effect of local oxygen tension on redistribution or shunting of blood as occurs in the normally functioning lung.

The magnitude of blood flow from systemic vessels entering the lung must obviously be of importance. The larger the blood flow the greater the chances of vascular congestion, hemorrhage, and susceptibility to superimposed pulmonary infection.

In some reports the anomalous arteries to the lung from the aorta or its branches have been described as having walls like that of other systemic vessels, but others have been described as thickened pulmonary arteries. Degenerative

changes and atherosclerosis have been demonstrated in such anomalous vessels even in young individuals. Aneurysm formation and rupture may occur. Hemorrhage into the lung may occur.[1, 2] One of my adult patients had a long history of raising a pinkish frothy sputum. The 12-year-old girl who complained of dyspnea on exertion was relieved of that complaint by ligation and division of the two systemic arteries which supplied part of the blood flow to her hypoplastic lung. I have assumed that her sensation of dyspnea was due to a localized area of pulmonary congestion.

SUMMARY

The pulmonary vascular plexus at one stage of embryologic development has important dorsal branches from the aorta which normally disappear. These vascular communications with the aorta or its branches may persist when there is faulty development of the pulmonary artery.

Although most recently reported cases of anomalous systemic arteries to the lungs have been discovered because of the associated presence of bronchiogenic cysts, bronchiectasis or sequestration of lung tissue, anomalous arteries from the aorta or its branches may enter grossly normal pulmonary tissue. Anomalies of the bronchial branching and lobar development may also be present.

The clinical features and the radiologic findings in cases of absence of the pulmonary artery to one lung are presented with illustrative examples.

Two cases with a hypoplastic lung receiving a considerable blood flow through systemic arteries are discussed. The effect of ligation of these systemic arteries is reported.

The clinical and physiologic questions which anomalous vascular communications to the lungs present are briefly considered.

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DISCUSSION

DR. JOHN S. HARTER, Louisville, Ky.—I wonder if Dr. Maier would consider the possibility of this type of case explaining the so-called capillary gear cell mechanism which was argued before this Association by Yates and Graham in one of the meetings in the early 1920's: that is, partial collapse of the lung due to lack of pulmonary circulation.

DR. CHARLES T. READ, Phoenix, Ariz.—I would like to discuss a case similar to the ones presented by Dr. Maier. This 8-year-old child was operated on two years ago and presented a combination of xanomalies, as did his cases. There were absence of the right pulmonary artery, agenesis of the right upper and middle lobes with hypoplasia of the right lower lobe, systemic artery supplying the hypoplastic right lower lobe, with abnormal venous drainage into the inferior vena cava which produced a very marked vascular shunt thereby. In addition there were retroesophageal arteries producing marked dysphagia. The child had been a feeding problem all her life and was unable to swallow large boluses of food or firm food. There was also a patent ductus arteriosus on the left side.

The esophagram indicated creasing which would lead one to believe there was some blockage producing dysphagia. There is a rather bizarre type of bronchial distribution showing absence of the upper and middle lobe bronchi. The angiocardiogram shows the absence of the right pulmonary artery; and another view at a later stage shows the right ventricle, the left auricle filling.

Following the removal of a right hypoplastic lung associated with the numerous bronchiovascular anomalies including an absent pulmonary artery, retroesophageal arteries and systemic circulation of the right lower lobe, a patent ductus arteriosus remained on the left side. About four months after the first operation, with only the left lung remaining, the patent ductus was approached through an anterior thoracotomy, divided and sutured. There was marked improvement in the patient after surgery.

So far as can be ascertained, this is the first time the correction of a patent ductus has been accomplished with only one lung present.

DR. I. M. MADOFF, Boston, Mass.—I have enjoyed Dr. Maier's excellent paper. He has contributed a great deal to our understanding of these interesting pulmonary circulatory anomalies.

Dr. Strieder, Dr. Gaensler, Dr. Lynch, and I have had occasion to study two patients with this anomaly. The first was a 14-year-old girl, who was symptom-free, but this chest film shows an abnormal upper mediastinal shadow. Some of our studies on this patient have been reported previously.

Angiocardiography shows an absent right pulmonary artery with a normal and slightly enlarged left pulmonary artery. This patient was studied by bronchospirometric technique, as well as by cardiac catheterization.

The right lung was seen to take up 7 per cent oxygen and the left lung took up 93 per cent. Supplying room air to both lungs, the right lung took up no oxygen, as opposed to 100 per cent on the left. Again, supplying oxygen to the right lung, and room air to the left, the right took up 18 per cent oxygen, as compared to 82 per cent on the left. By applying the technique suggested by Drs. Bloomer, Harrison, Lindskog and Liebow, of New Haven, it was possible to calculate that the effective bronchial circulation through the right lung was 17 per cent of the total systemic output of the left ventricle, as opposed to 1 per cent, which should be the normal output through the bronchial circulation of this lung.

A 23-year-old white man was studied because of cyanosis and dyspnea. He had been in good health until the age of 19 and, prior to that time, had had no external stigmata of any disease. The angiocardiogram shows an absent right pulmonary artery and a large left pulmonary artery. He was in mild congestive failure at this time and the circulation was very slow.

This patient died several months later. At autopsy, there was a patent ductus arteriosus and an infantile type of coaretation of the aorta. There was no anomalous

artery to the right lung and the bronchial arteries did not appear to be enlarged. The parenchyma of the right lung was normal on microscopic examination, whereas that of the left lung showed marked atherosclerosis of the pulmonary vasculature, apparently due to shunt. Interestingly enough, this patient had clubbing of both feet and the left hand, but not the right hand.

The oxygen uptake of the right lung was 16 per cent, as opposed to the first patient, where it was 7 per cent, suggesting that where the circulation of the left lung was impaired, and the oxygen uptake was impaired, the normal bronchial circulation of the right lung would take up 16 per cent of the oxygen.

DR. DAVID H. WATERMAN, Knoxville, Tenn.—We have had the opportunity of seeing two of the latter type of cases that Dr. Maier described, of the rudimentary lung and very small pulmonary artery. Both cases were found on routine x-ray surveys, and both were completely symptom-free. The first was an automobile mechanic doing heavy work and the other was a teen-age boy who was a member of his local basketball team. The x-rays of both these patients looked very much like those of the patient shown by Dr. Read, the pathology being on the right side in each instance. I would like to ask Dr. Maier if this condition is not more commonly found affecting the right side rather than the left.

The amount of lung tissue present was exceedingly small. In the first case a single lobe measuring 6 cm. in length was encountered. Pneumonectomy was performed. In the second case there was a lower lobe, a rudimentary middle lobe with severe saccular bronchiectasis, and absence of the upper lobe. In this case we resected the rudimentary middle lobe and ligated the systemic artery leading to the lower lobe, in line with Dr. Maier's suggestion. Both patients have continued to do well.

DR. HERBERT C. MAIER (Closing).—I wish to thank the discussors. With regard to the question of shrinkage of the lung being related to changes in circulation, I believe this is a very important and interesting correlation. There is, as has been shown also by others who have ligated a pulmonary artery and left the lung in, a tendency for such a lung to reduce in volume. I wondered whether some of the microscopic changes seen in the lung which we removed might not have been due rather to the circulatory derangement than to superimposed infection.

These cases of absence of the pulmonary artery are considerably more common on the right side than on the left. This is true whether the case is without heart disease, or whether you are dealing with cases where it is in association with the tetralogy of Fallot.

SURGICAL RECONSTRUCTION OF THE SUPERIOR VENA CAVA

J. GORDON SCANNELL, M.D., AND ROBERT S. SHAW, M.D. (BY INVITATION)
BOSTON, MASS.

IT IS unusual to find superior vena caval obstruction that lends itself to surgical relief. The great majority of such cases are the result of inoperable malignancy, and for this x-ray treatment is our best recourse. There is, however, a small group of individuals in whom superior vena caval obstruction is the result of some benign process. As a general rule in the latter group, the symptoms are not disabling or particularly distressing, but exceptions occur where the disability may be considerable and the discomfort intolerable, as in the two individuals reported here. For these patients reconstruction of the superior vena cava by means of a free vein graft is proposed.

In 1948 Gerbode and his associates[1] demonstrated in the experimental animal the feasibility of anastomosing the superior vena cava to the auricular appendage. In 1951, Klassen, Andrews, and Curtis[2] described one patient suffering from superior vena caval obstruction in whom a free vein graft was placed successfully between the azygos vein and the right atrium in an effort to relieve obstructive symptoms. Other than these two, the literature contains only sporadic reports of attempts to relieve superior vena caval obstruction by operative measures, either "decompression"[3] or lysis of constricting scars.[4, 5] Neither of these maneuvers would have been of value in the two patients reported here.

CASE 1.—A. C. (M. G. H. No. 695943) was a 53-year-old man. Three years before his current admission he had received x-ray treatment (3,500 r) to a right superior mediastinal mass which had caused moderate pressure symptoms (Fig. 1). Contrary to our established practice, this treatment had been given without an actual biopsy. The immediate response to radiation was excellent (Fig. 2). The pressure symptoms were relieved for about one year but the patient then began to suffer from congestion of his head and neck, so severe that he was unable to follow his usual occupation of carpenter. He complained of severe headaches, dizzy spells, and occasional "black-outs." The symptoms were entirely disproportionate to the moderate degree of arterial hypertension that he had. X-ray films of his chest showed no evidence of recurrence of his mediastinal tumor. The physical findings were those of the classical superior vena cava syndrome. The veins of the head, neck, and arms were distended and tortuous; there were persistent orbital edema and fullness of the neck. The pressure in the antecubital vein was 21.0 cm. saline. The extent of the venous collateral is shown in the accompanying venograms.* Seventy per cent diodrast was injected first into the right

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Read at the Thirty-fourth Annual Meeting of The American Association for Thoracic Surgery at Montreal, Quebec, May 3 to 5, 1954.

*Venograms in Case 1 were made by Dr. Clifford Straehley.

Fig. 1.

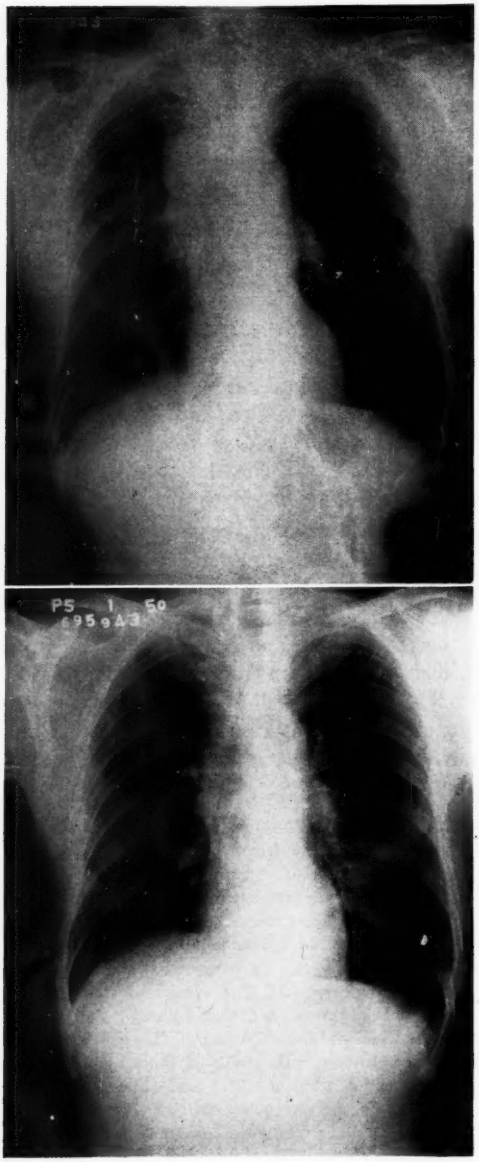

Fig. 2.

Fig. 1.—Case 1. X-ray film of chest demonstrating mass in right superior mediastinum before response to x-ray therapy, three years prior to operation.

Fig. 2.—Case 1. X-ray film of chest taken one month after x-ray therapy (3,500 r) showing marked regression of superior mediastinal mass. Status was essentially unchanged three years later, immediately prior to operation.

Fig. 3.

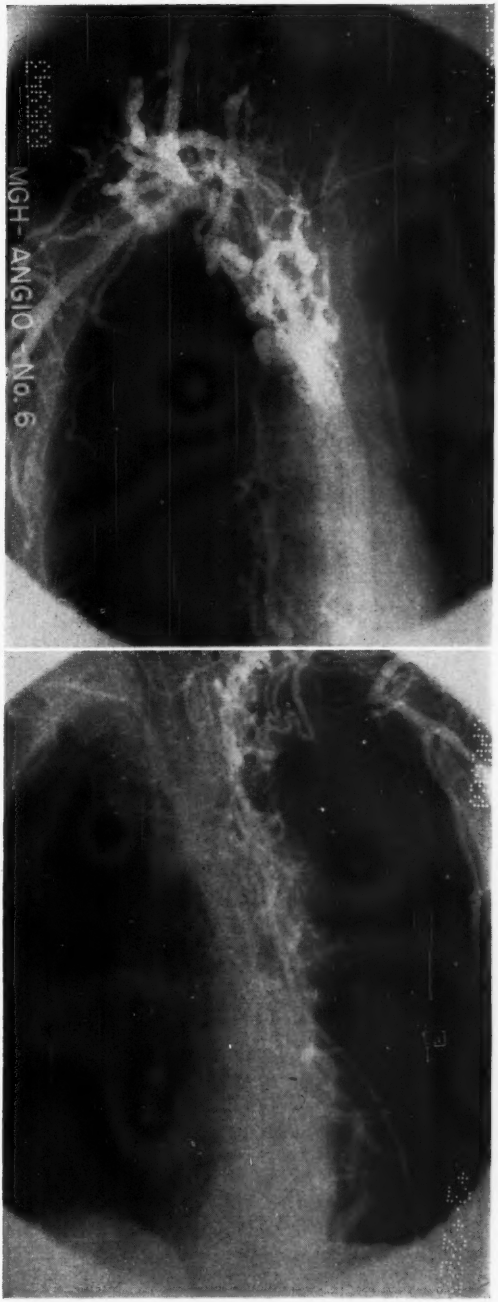

Fig. 4.

Fig. 3.—Case 1. Venogram with 70 per cent diodrast injected into the right antecubital vein showing extensive collateral circulation with no identifiable superior vena cava or innominate vein. Passage of dye into azygos system appears to be by way of the superior intercostal vein.

Fig. 4.—Case 1. Venogram with 70 per cent diodrast injected into left antecubital vein. There is striking visualization of the left pericardiophrenic vein. No innominate vein can be seen.

antecubital vein (Fig. 3), then into the left (Fig. 4), and finally into a superficial femoral vein in order to outline the cardiac end of the superior vena cava (Fig. 5). The lumen of the superior vena cava was completely obliterated at and above the level of the azygos vein. To provide symptomatic relief by improving the drainage from the superior caval system, it would be necessary to re-establish continuity between a distal major vein and the right atrium, either the auricular appendage or preferably the intrapericardial portion of the superior vena cava. The severity of the patient's symptoms was judged sufficient to warrant operation, which was carried out on March 13, 1952.

The plan of operation is indicated in Fig. 9. Through a median sternotomy incision the superior mediastinum and base of the neck were exposed. The superior vena cava and both innominate veins were encased in and obliterated by dense scar tissue. There was no

Fig. 5.—Case 1. Venogram with 70 per cent diodrast injected into a superficial vein to demonstrate the intrapericardial portion of the superior vena cava by reflux of the dye from the right atrium. Auricular appendage cannot be identified with certainty.

evidence of residual tumor. Once through the skin and subcutaneous tissues there was remarkably little difficulty with venous bleeding. The key to the operative approach lay in the pericardial sac, for within this sac the structures were virtually normal (Fig. 6) and the intrapericardial portion of the superior vena cava was of generous length (see venogram, Fig. 5). A free vein graft, in this case the superficial femoral vein, taken from the same patient and transferred almost immediately to the chest, was used to bridge the gap between the right jugular vein and the right atrium (Fig. 7, *A* and *C*). Dilute heparin solution was injected into the lumen of the vein graft. It was reasoned that anastomosis of one internal jugular vein to the atrium would carry sufficient blood from the head and neck to reduce the venous congestion in the region of maximum symptoms. It was further anticipated that this diversion of a sizable volume flow of blood would reduce the load on the already established collateral circulation and in this way reduce congestion in the entire superior vena caval drainage area as well.

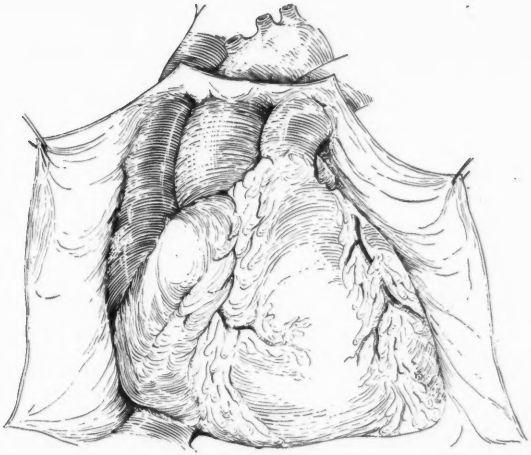

Fig. 6.—Drawing from autopsy observation showing the normal appearance of the superior vena cava within the pericardial sac. (After Holman et al.: Surg., Gynec. & Obst. 89: 129-144, 1949. By permission of Surgery, Gynecology and Obstetrics.)

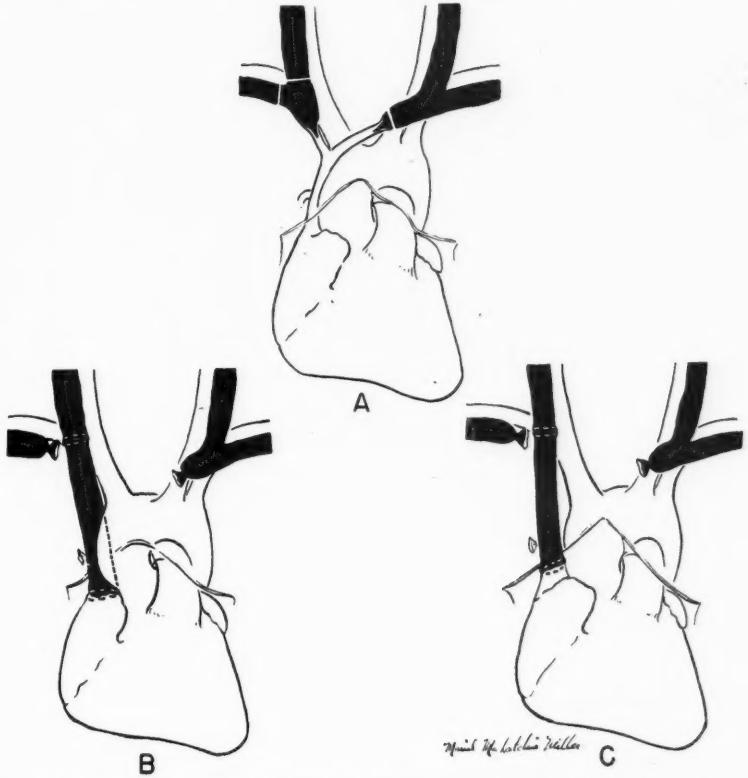

Fig. 7.—Diagrams to demonstrate the pathological problem (*A*), and the method of solution (*B* and *C*). In Case 1, a free vein graft was placed between the right internal jugular vein and the intrapericardial portion of the superior vena cava (*C*). In Case 2 the graft was placed between the internal jugular vein and the right auricular appendage.

The immediate postoperative course was gratifying. Unfortunately, and certainly unwisely in view of the fact that the area had been previously irradiated, the sternum was closed without wire. The closure proved to be unstable, and forty-eight hours postoperatively partial dehiscence of the incision occurred. In spite of resuture and the liberal use of antibiotics the patient developed an anterior mediastinitis and pericarditis from which he died on the eighth postoperative day. Post-mortem examination disclosed the important fact that *the vein graft, in spite of the mediastinal sepsis, was perfectly patent.*

CASE 2.— E. D. (M. G. H. No. 631572) was 33 years old. Twelve years before operation he had sustained a severe chest injury in a fall from a staging. Two years later he began to suffer from choking spells, great congestion of his face and neck, and "black-out" spells. In 1948 the patient was first admitted to the Massachusetts General Hospital, and obstruction to the superior vena cava at the level of the azygos vein was demonstrated by venography and later by the passage of cardiac catheters (Fig. 8). Operation was postponed until the techni-

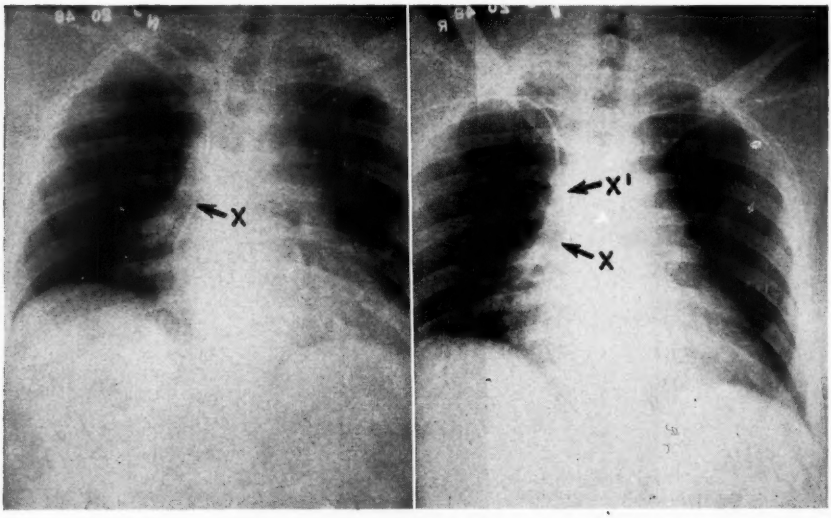

Fig. 8.—Case 2. Preoperative chest films. In the left-hand film a cardiac catheter has been introduced by way of a saphenous vein to the level marked *X*. In the right-hand film, the lower limit of the innominate vein is demonstrated by a catheter introduced into the right antecubital vein (X^1). Venograms were unsatisfactory for reproduction.

cal details could be satisfactorily worked out. The patient dropped from sight, but returned to the hospital in August, 1952, with the complaint that his choking sensation and congestion were much worse and now intolerable. There was striking distention of the superficial veins of his face, neck, and arms. He was unable to lie flat for more than a few seconds without appearing almost asphyxiated, nor could he bend forward while seated in a chair for more than 35 seconds without producing a frightful appearance of congestion. The venous pressure in his right arm was 27.4 cm. saline.

Operation was carried out Sept. 11, 1952. The plan was basically the same as in Case 1, except that in this case it was necessary to implant the cardiac end of the vein graft into the tip of the right auricular appendage (Fig. 9). The latter was easily controlled with a soft, noncrushing clamp. Dilute heparin solution was used locally. No anticoagulants were used postoperatively.

In this second case, great difficulty was encountered with venous collateral and dense scarring of the superior mediastinum. Scattered calcification throughout the scar suggested

that the pathologic process was an organized hematoma of the superior mediastinum, traceable to the original chest injury.

Though complicated by atelectasis, the patient's course was satisfactory and he was discharged on the seventeenth postoperative day. The patient returned for evaluation three months later. Subjectively he had improved greatly. He could sleep flat without choking distress or nightmares. He could bend over to tie his shoes or to take things out of a lower drawer—a motion necessary to his occupation as a salesman in a jewelry store. He could lie flat on the examining table quite comfortably and with minimal congestion of his face. Three minutes after bending over while seated in a chair his face appeared red, but not abnormally

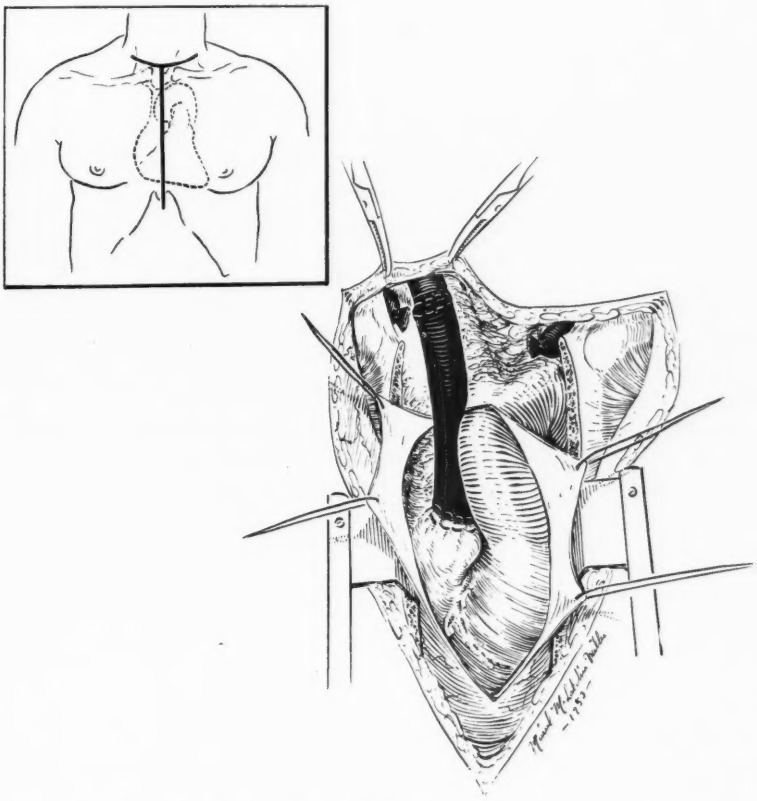

Fig. 9.—Case 2. Operative sketch. Details of anastomosis omitted. A combination of everting continuous and interrupted mattress sutures of five-0 silk was used. The anatomic relationship of the graft to the ascending aorta and to the upper limits of the pericardium is indicated.

so. The venous pressure in his right arm was 23.6 cm. saline, only slightly lower than the preoperative values. This was judged to be of limited significance since operation did not directly decompress the subclavian vein. Objective evidence of the patency of the vein graft was obtained by venography (Fig. 10).

The patient was last seen one year postoperatively. His general clinical improvement was well maintained.

Fig. 10.—Case 2. Venogram, three months postoperative. Diodrast injected into right internal jugular vein percutaneously. Films taken at approximately one-half second interval showing passage of dye through graft and prompt clearing of opacity. Slight constriction evident at level of upper suture line.

CONCLUSION

So far as we are aware, these two cases, plus the one somewhat similar case reported by Klassen et al., are the first patients in whom a direct attempt to relieve superior vena caval obstruction by free vein graft has been carried out. Credit for many of the details of the technical approach must go to Gerbode and his associates. It is unlikely that the procedure will have wide application, but in the occasional case where the symptoms are sufficiently distressing and disabling, and where a benign or stationary basis for the obstruction can be shown, it appears to be logical and justifiable.

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DISCUSSION

DR. PAUL C. SAMSON, Oakland, Calif.—I think Dr. Scannell should be congratulated on these two cases and on carrying experimental work into the clinical field. Such cases represent a small but growing number of patients in whom significant clinical mediastinal lymphad-

enitis is manifest. I have been particularly interested in this problem because the vascular system is involved as well as the tracheobronchial lymph nodes.

My own case was not entirely successful, but luckily I had the opportunity of talking with Dr. Frank Gerbode at some length before treatment was attempted. This 18-year-old man entered the hospital in November, 1948, about three weeks after having had a tooth pulled; we do not know the significance of that. There was rapid development of weakness, of swelling in the upper extremities and the face, fever and pallor and cyanosis.

No lymph nodes were seen by x-ray. For three months the patient was treated by intensive chemotherapy and bed rest, and several x-ray treatments were given because of the presumed diagnosis of lymphoma. We did not see him until just before surgery. His venous pressures were consistently elevated from 200 to 400 mm. of water. The obvious obstruction continued, and on May 14, 1949, an anterior mediastinotomy was done which revealed a great amount of scar tissue and many large and small lymph nodes matted together. Some of them contained caseous debris. There was actually a rosette of nodes around the entrance of the superior vena cava into the pericardium. Following our discussion with Dr. Gerbode we used an autograft of superficial femoral vein, end-to-end above and end-to-side below. This was not completely successful. Although there was considerable relief of the symptoms, no particular diminution in the venous pressures had occurred five months following operation.

Something happened in the venogram, which I cannot explain. The azygos system was full postoperatively, but did not fill preoperatively. Time will not permit the discussion of everything we learned from this case. If, however, I had to do such a case again, I would do a posterior right thoracotomy incision instead of anterior mediastinotomy, because I believe that, in certain cases at least, the azygos vein may be used as a swing-up graft rather than to have a completely separate autograft.

DR. T. J. O'NEILL, Philadelphia, Pa.—I should like to comment on this paper briefly and to present two patients who had superior vena caval obstruction due to benign lesions.

The first patient had had symptoms of complete obstruction for a period of twenty years. The original diagnosis was said to have been tuberculosis but it was never proved, and on the planogram we can see calcification of the superior vena cava and its two major confluences and a calcified lesion in the lung. This patient has a pressure of 45 cm. in the upper veins. She was recently admitted to the hospital. There is tremendous swelling of the head and arms and it appears that she will be a candidate for vein graft such as Dr. Scannell has so well outlined.

The next patient was an instance of almost complete obstruction of the superior vena cava. This woman had symptoms for almost ten years. The symptoms began after an exploratory operation done elsewhere on the right chest. The operative report was not complete, the findings were not mentioned, and the only thing we could tell was that apparently there was a nonfunctioning lung on the right side as the dye outlined the left pulmonary artery well and none got into the right side. There was a tremendous woody mediastinitis present. An exploratory operation was done and it was found that an obstruction existed in this area; it was thought that a vein graft was not necessary. The vein was opened and the well-organized scar of thrombuslike material was rongeured from the inside of the vein; the vein was reconstructed, with subsequent disappearance of symptoms over the past year. I think there is a possibility of directly scraping out the vein in patients who have a short length of obstruction. Where a long length exists, I believe that vein graft will be the only permanent solution.

DR. EARLE B. KAY, Cleveland, Ohio.—I should like to comment on this paper, not from the standpoint of successes but of failures. Following Dr. Gross's work in 1948 we performed a series of experiments to determine whether vena caval transplants might work.

The initial success was relatively good. The vena cava was taken from one dog and transplanted between the junction of the innominate veins and the auricular appendage of another.

Venograms taken from four to six months postoperatively showed a patent graft in approximately 30 per cent of the dogs. At that time we were about to present this before this Association.

We have here an example of a patent vein graft at twelve days. By six months all the grafts showed varying degrees of sclerosis. At the time the dogs were sacrificed none showed what we would describe as good grafts.

During the period of initial success three patients with superior vena caval syndrome secondary to chronic fibrosing mediastinitis were operated upon. The first patient died postoperatively following a transplant taken from another individual dying in an accident, which was anatomosed between the innominate veins above and the auricular appendage below. The second patient had a preoperative venous pressure of 45 cm. of saline. An anastomosis was made between the azygos vein and the auricular appendage. Postoperatively the pressure dropped to 15 cm. of saline. There was gradual return of the venous pressure to the preoperative level. The patient died four months postoperatively. The anastomosis had sclerosed. The third patient, with a similar condition, had a superficial femoral vein transplanted between the innominate veins at their junction and the auricular appendage. That patient is alive today, about five years later, but there is evidence that the graft is not functioning. From our experience we would state that the homologous or autogenous transplantation of veins in the treatment of superior vena caval syndrome secondary to chronic fibrosing mediastinitis is not successful.

DR. ROLLINS HANLON, St. Louis, Mo.—I would agree in general with the criteria of Dr. Scannell and his associates that this procedure should be employed in benign conditions in which the patient's symptoms are severe. But I would like to suggest that there are circumstances in which, with a malignant obstruction, even an irremovable malignancy, the symptoms may be so severe that it might be considered expedient to carry out a palliative shunt. That was the circumstance in a 65-year-old man whom we saw four years ago, who presented the picture described by Dr. Scannell of such severe vena caval obstruction that he was unable to remain in any position except bolt upright; the slightest tendency toward recumbency produced alarming signs and symptoms. For that reason, with a working diagnosis of malignancy, we explored him through a combined sternotomy and intercostal incision. The diagnosis of malignancy was confirmed; the condition was an irremovable malignancy with infiltration of the entire dorsal surface of the vena cava from its origin down to and including the intrapericardial portion. For that reason it was not possible to circumscribe the superior vena cava at any point so as to excise the involved area and replace it by a graft between its cut ends. We therefore placed an aortic graft with its caudal portion anastomosed to the tip of the right auricular appendage and its cephalic end placed tangentially into the ventral surface of the superior vena cava.

End-to-end anastomosis of the graft to the right auricular appendage was done and a button of the ventral wall of the cava was excised distal to a curved Potts multitoothed clamp, applied tangentially. The graft was preserved according to the original technique of Gross, Bill, and Peirce and was kindly furnished by Dr. Peirce.

The graft carried blood around the obstructed area. As soon as the clamps were removed there was a striking decrease in venous tension in the upper part of the body.

The angiogram confirms the patency of the graft; one may see contrast substance flowing through it and appearing promptly in the pulmonary artery.

The patient was promptly relieved, his venous pressure fell from a preoperative level of 320 mm. of saline to 180 a few hours after operation, and to 100 some days later. He lived for about four months and, despite x-ray therapy, the graft remained patent as judged by a persistent murmur.

DR. KARL P. KLASSEN, Columbus, Ohio.—We agree with Dr. Scannell that most of these cases of benign constricting type of occlusion of the superior vena cava, whether produced by tuberculosis or fungus infection, do not require treatment. However, we did have two patients who did require treatment because of the severity of their symptoms. The first one was mentioned by Dr. Scannell. This patient is still in good health; his pressure, however, has not returned to normal. We believe the graft to be patent although we have not proved this by venography. It was proved patent when this patient was reported in 1951.

The second patient had severe symptoms produced by a benign constricting lesion of the superior vena cava. The obstruction extended over a distance of about 10 cm. and a vein graft could not be applied. For this reason we elected to use a preserved aortic homograft. This was used to replace the vena cava with immediate return of flow through this channel and a fall in the venous pressure in the upper extremities. However, one month later this graft clinically became thrombosed. The patient is all right two years later, his graft is not functioning. He has developed more extensive collateral circulation and is able to carry on as a laborer.

DR. RALPH A. DETERLING, New York, N. Y.—We also anticipated a need for an occasional replacement of the superior vena cava, and late in 1951 Dr. Vance Lucas and I carried out some experiments on dogs, excising segments of superior vena cava and implanting aortic homografts preserved in a nutrient electrolyte solution at 4° C. A series of animals prepared in this manner were followed by angiography and in no instance was there a disappointing result. Microscopically, there was disappearance of the cellular elements of the graft, there was excellent epithelization, and the suture line looked quite good. In some instances after a long period there was corrugation of the graft.

One graft was maintained in a dog for seven months, to demonstrate such a change. Then, for two years we awaited a patient for whom this might be suitable. We explored a number of patients with caval obstruction who turned out to have carcinoma of the thymus, Hodgkins' disease, or aortic aneurysms. Finally, in January, 1954, we saw a 36-year-old woman who had been treated for angioneurotic edema for eight months, with moderately severe symptoms. She had a pressure in her brachial veins of 300 mm. of water. A venogram showed complete obstruction of the superior vena cava, and on January 12 we explored her very adequately through a right posterior incision as suggested by one of the discussors.

A preserved aortic homograft was used to bridge a 6 cm. defect after excision of an obstructed segment of vena cava. The obstruction resulted from an old tuberculous lymph node. The graft was anastomosed to the intrapericardial portion of the vena cava adjacent to the auricle, as shown in this area. We contemplated using the tip of the appendage as suggested by Gerbode and his group, but the motion was very active and we feared that thrombosis might occur. The results so far, after five months, have been very satisfactory. Anticoagulant drugs were not used.

DR. FRANK L. GERBODE, San Francisco, Calif.—I should like to congratulate Dr. Scannell on the excellence of his presentation, and also upon his ability in finding two patients with correctable caval obstruction. We have searched for these patients rather diligently and find that they are extremely scarce.

I thought you might like to know what has happened to some of the experimental work which Dr. Scannell and others have mentioned. We have now followed some of the animals who had experimental atriocaval shunts for more than five years. I can give you the results of some of these shunts after that period. In a superior caval shunt, the superior vena cava was moved over to the auricular appendage, and appears smooth and after two and a half years. In an inferior caval shunt, the inferior vena cava was detached from the right atrium and made to enter the left atrium. A small line is the only evidence of the suture line. If such a shunt stays open during the immediate healing stage, it apparently will stay open forever.

In another series of animals, about 25 in all, we used homografts, very much as suggested here this morning, to bridge an experimental defect in the superior vena cava. In every instance in which we used an aortic homograft, thrombosis or gradual fibrosis occurred. We also did six vein homografts, and these also fibrosed or scarred down in time. As I have stated previously, in order for a vessel homograft to remain patent, systemic blood pressure is necessary. It acts as a stent over which the host replaces the graft. Venous pressure is not great enough to serve in this way. For these reasons I do not think using a homograft is the answer; what Dr. Scannell has suggested is far better.

There is another situation where the principle of atriocaval shunt can be applied, that of abnormal venous return to the heart. Both main pulmonary veins join a common vein which develops into a persistent left superior vena cava, carrying the blood to the right side. In order

for this situation to be compatible with life, a patent foramen ovale must be present to allow the blood to pass to the left side of the heart. The auricular appendage lies conveniently next to this large vein, making a side-to-side shunt feasible. We attempted to shut off the cava after the shunt was completed, but the heart did not seem to tolerate this too well. The child has done extremely well, is growing normally and, although we cannot say for certain that the shunt is functioning, her clinical course has been excellent.

DR. C. W. HOLMAN, New York, N. Y.—I should like to comment about a patient on whom we did a shunt procedure using a preserved arterial aortic graft. The reason for reporting this is because I thought that a preserved arterial graft would be superior to a vein graft.

I think from the discussion of Dr. Gerbode and Dr. Klassen, it seems that possibly a vein graft is superior to the aortic graft which we used. This venogram tells the story of the obstruction of the superior vena cava in the region of the right innominate vein. Here is a sketch of what was found in the angiocardiogram. At operation we found a condition typical of the mediastinitis reported by Erganian and Wade. The left innominate was lost in the process, the obstruction extending to the right innominate vein. Here is shown the aortic graft in place. The pressure dropped from the preoperative level of 360 mm. of saline to 110. Along the lines of Dr. Gerbode's and Dr. Klassen's comments, the venous pressure is now increased to about 180 mm. after a period of about six months. This shows the angiocardiogram after insertion of the aortic graft. The patient is completely asymptomatic.

DR. J. GORDON SCANNELL (Closing).—I would merely like to thank the discussors. I have nothing to add.

PULMONARY BLASTOMYCOSIS

A Critical Analysis of Medical and Surgical Therapies, With a Report of Six Cases

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A RATIONAL and optimistic therapeutic approach to pulmonary blastomycosis is now possible. A safe, effective chemotherapeutic agent is available and pulmonary resection may be employed when indicated. This report will review the accumulated experience with stilbamidine and 2-hydroxystilbamidine therapy and will analyze the reported (20 cases) and personal (6 cases) experience with pulmonary resection in this disease.

The hypomycete, *Blastomyces dermatitidis,* causes cutaneous and visceral lesions with equal frequency.[1] Gilchrist[2, 3] in 1894 first described the disease in its cutaneous form. The dermatitis is relatively benign, but the mortality in *recognized* cases of visceral disease has, until recently, been approximately 90 per cent.[4] The lungs are involved most frequently, then the skeletal system, but lesions have been found in every organ and tissue of the body.[4, 5] There is evidence that the lung is the portal of entry at least in the systemic disease.[4, 5] There is pathologic evidence that even without specific therapy there is a strong healing tendency in the lungs.[5] It is probable that unrecognized and self-limited cases have occurred.

INCIDENCE

Blastomycosis is not uncommon in some localities although it is generally considered a rare disease. It has been reported almost exclusively from North America, but cases have been reported from China,[6] England,[7] Australia,[8] and recently in epidemic proportions from Okinawa.[9] Early in the century the disease was reported most commonly from Chicago and the Midwest.[4, 10] Subsequently numerous cases have been reported from Cincinnati,[5] Buffalo,[11] New Orleans,[12] Memphis,[13] and Durham.[1] In 1939 Martin and Smith[4] collected 243 proved and presumptive cases.

The disease is being recognized more frequently. Seabury[14] has seen and treated 12 cases of systemic blastomycosis at the Charity Hospital in New Orleans in the last two and one-half years. In 1949 Smith[1] reported that 50 cases had been studied in The Duke Clinic in the past eighteen years. Sealy and

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Smith[15] report that they have recently seen from a single small community in eastern North Carolina 8 cases of pulmonary blastomycosis, three being children living in the same block. Between 1951 and 1953 White and Owen[16] resected 4 unsuspected lesions of pulmonary blastomycosis in the comparatively small city, Huntington, West Virginia (pop. 80,000).

The incidence of the disease to a large degree parallels the interest and suspicion of the medical profession of a locality. Snapper and McVay[13] reported 16 cases, 5 cutaneous and 11 systemic, seen at the John Gaston Hospital in Memphis over a ten-year period. With increased medical interest in the disease, 7 additional cases were seen in the subsequent fifteen months. Hughes and co-workers[17] report an almost fourfold increase in the diagnosis of all pulmonary fungus diseases at the Kennedy Veterans Administration Hospital in Memphis since 1949 when the staff became interested in the problem.

CLINICAL PICTURE

Pulmonary blastomycosis most commonly develops as an indolent chronic infection causing systemic symptoms of fever, malaise, night sweats, and weight loss, as well as thoracic symptoms such as cough, sputum, hemoptysis, dyspnea, and chest pain (Table I). The pulmonary infection may be protean

TABLE I. PRESENTING SYMPTOMS IN 6 CASES OF PULMONARY BLASTOMYCOSIS TREATED BY RESECTION

CASE	COUGH	TEMPERATURE	CHEST PAIN	HEMOPTYSIS	MALAISE	WEIGHT LOSS (LB.)	DURATION OF SYMPTOMS	SKIN LESIONS
1		102°	+		++	11	2 mo.	
2	+	102°		+	+	20	7 wk.	
3	+		+	+			27 mo.	
4	+	101°					3 mo.	
5	+	101°	+	+	+	24	2 mo.	
6	+	101°			+	10	12 mo.	+

in its manifestations. Cases of acute and subacute pneumonia have been observed.[9, 18] We have observed an acute blastomycotic lung abscess in a 12-year-old boy. There may be associated lesions in the skin, the subcutaneous tissues, or the viscera.

PATHOLOGY

Schwarz and Baum[5] made a careful pathologic study of 20 cases of pulmonary involvement from Cincinnati and the Armed Forces Institute of Pathology. They classified the lesions into three groups. (1) Seven cases presented primarily an exudative pneumonia without granuloma formation. Alveolar destruction was common but major abscess formation was rare. Blastomycetes were frequent. (2) Four cases consisted chiefly of granulomatous lesions with epithelioid cell tubercles. Giant cells were a prominent feature. Yeast cells were less frequent. (3) In 9 cases mixed exudative and granulomatous lesions were present. A pleuritis was found in all cases in which pleura was available for examination, but the absence of pleural

fluid was notable. Endobronchial lesions, chiefly in the smaller bronchi, were seen in all but one case. A tendency to scarring was seen repeatedly and was interpreted as evidence of healing. Cavities were not observed, but focal necrosis occurred in the center of large exudative foci.

Martin and Smith[4] report that the pathologic picture is quite variable. They describe diffuse or focal consolidation which may simulate miliary tuberculosis or there may be larger nodules or abscesses distributed through the organ. They state that cavities occur but that they rarely exceed 1 cm. in size. Caseation is described frequently in small foci.

In view of the repeated pathologic observations that large cavities do not occur, it is interesting that in our Case 3, J. R. T., the presenting lesion was a cavity in the left upper lobe which enlarged over a two-year period and at resection measured 4 cm. in diameter. Our Case 6, C. McC., developed cavitation and complete destruction of the left lower lobe, although advanced bilateral disease was otherwise controlled by 2-hydroxystilbamidine therapy. Feld and Cadden[19] report in two cases cavities measuring 5 and 7 cm. in diameter. Murphy[20] resected a right upper lobe for a 2 cm. cavitary lesion thought to be an abscess. He has treated a second case medically for bilateral cavitary disease. Seabury[14] has treated a case with a destroyed right upper lobe, two large cavities in the apex of the right lower lobe, and multiple cavities in the upper and lower lobes on the left (see Case L. M.). Tissue destruction and cavitation occur less frequently than in tuberculosis, but extensive necrosis and cavitation may occur.

The disease may involve the chest wall directly or by metastasis, but there is little tendency for cutaneous fistula formation so commonly seen in actinomycosis. Generalized spread throughout the body may be expected at any time. The fungi have been seen repeatedly in the blood vessels and this is the route of spread of the disease.[5]

DIAGNOSIS

The problem of correctly identifying a lesion in the lung is the same in blastomycosis as in other pulmonary disease. Awareness of the disease is an essential prerequisite for a correct diagnosis. The clinical picture is not diagnostic. Even when one is aware of the possibility and uses every test at his command, correct preoperative diagnosis is often difficult.

Roentgenography.—There is no characteristic pattern. Every type of picture from widespread bilateral disease to solitary coin lesions has been seen. Since the disease is a granuloma, it must be considered with, and differentiated from, tuberculosis, coccidioidomycosis, moniliasis, histoplasmosis, and torulosis.[9] Three of our cases were thought to be inflammatory, two neoplastic and one cystic disease.

Bronchoscopy.—Weisel and Landis[21] have reported seven consecutive cases of blastomycosis with endobronchial disease. The characteristic findings were superficial mucosal erosions and glairy, thick brown mucus. One case

TABLE II. TABULATION OF REPORTED AND PERSONAL CASES OF PULMONARY BLASTOMYCOSIS SUBJECTED TO RESECTIONAL THERAPY

AUTHOR DATE	IN-ITIALS	AGE	COLOR SEX	PREOP. DIAGNOSIS AND TREATMENT	RESECTED SPECIMEN	POSTOP. TREATMENT	RESULTS
Smith[1] 1949	M. M.	47	WF		Lobe	KI	Died 2 years after resection of disseminated disease
Smith[1] 1949	J. T.				Lobe	KI	No follow-up
Webb[37] 1949		36	WM	Undetermined	Right lung	None	Died day after surgery
Feld, Cadden[19] 1949	J. S.	30	WM	Blastomycosis, KI	Right upper lobe	KI	Died 11 months postop. of disseminated disease
Good et al.[38] 1951		39	WM		Lobe		No follow-up
Lowry et al.[39] 1951	W. C. B.	30	NM	Pulmonary cyst, no treatment	Right lower lobe	None	Five years' follow-up, patient well*
Hopkins and Murphy[24] 1952	V. R.	34	NM	Blastomycosis, no treatment	Right lung	KI	Died 6 months after resection of disseminated disease
Hopkins and Murphy[24] 1952	A. D.	40	WM	Carcinoma, no treatment	Left lung	KI, 6 weeks; undecylenic acid	Developed widespread skin dissemination, treated with undecylenic acid, alive and disease-free 2 years later*
Weisel and Landis[21] 1953	G. H.	27	WM	Undetermined, no treatment	Right lower and middle lobes	None	Three years and 10 months free of disease*
Weisel and Landis[21] 1953	H. B.	56	WM	Undetermined, no treatment	Right upper lobe	None	Four years free of disease*
Buechner et al.[25] 1953	A. P.	56	NM	Undetermined, no treatment	Right lower lobe	None	Two years free of disease*
Buechner et al.[25] 1953	F. L.	49	NM	Undetermined, Strep. P.A.S. 3 weeks	Right upper lobe	Human serum KI, 2-hydroxystilbamidine	Residual disease. Rib and transverse process involvement. Thoracoplasty, responded to medical treatment. Well 18 months later*
Cummins et al.[32] 1953		39	WM	Carcinoma	Right upper lobe	KI, stilbamidine	Developed skin lesions. Well 2 years

Hughes et al.[17] 1954	L. E. P.	40	WM		Left upper lobe		Thirty-three months free of disease*
Sealy et al.[31] 1954	C. W.	36	WM	Blastomycosis, blastomycin	Left upper lobe	Blastomycin, KI	Contralateral spread, responded to medical treatment. Well 3 years after surgery
Sealy et al.[31] 1954	J. H.	41	NM	Blastomycosis, blastomycin	Right lung	Blastomycin	Three years free of disease
White and Owen[16] 1954		60	WM	Carcinoma	Left lung	None	Generalized dissemination, died 6 days postop.
White and Owen[16] 1954		50	WF	Chronic suppuration	Right lower lobe	None	Died 18 hours postop. in staticus asthmaticus
White and Owen[16] 1954		60	NF	Carcinoma	Left lung	None	Well 14 months postop.
White and Owen[16] 1954		34	NM	Chronic suppuration	Right middle lobe	Stilbamidine	Suspected spread in right lung. Well 10 months later
Acree, DeCamp, Ochsner							
Case 1	J. T.	39	WF	Undetermined	Left lung	Blastomycin	Left 7th rib involved; thoracoplasty; died 2½ years later of cardiac arrest during rhizotomy
Case 2	C. D.	62	WM	Carcinoma, no treatment	Right lung	Blastomycin, KI	Questionable bronchial stump disease; 5 yr. 9 mo. free of disease
Case 3	J. R. T.	36	WF	Pulmonary cyst, no treatment	Left upper lobe	Blastomycin	5½ years free of disease
Case 4	J. S.	55	WF	Undetermined, no treatment	Right upper lobe	None	Died of coronary occlusion 5 months after surgery
Case 5	R. W. J.	37	WF	Undetermined, no treatment	Left upper lobe	None	Died in immediate postop. period; pheochromocytoma found at autopsy
Case 6	C. McC.	41	NM	Blastomycosis, 2-hydroxystilbamidine	Left lower lobe	2-hydroxystilbamidine	Eight months free of disease

*Personal communication from author.

had an endobronchial mass. We have seen one case with a 3 mm. endobronchial mass, but none of our operative cases had significant endobronchial lesions.

Sputum.—Smear and culture of the sputum is the ideal way of making a positive diagnosis. Unstained pus particles from the sputum, liquefied by potassium hydroxide, frequently reveal typical organisms. Diagnostic techniques are neither difficult nor costly,[22] but the organisms may be difficult to identify.

A positive skin test is considered significant when present, and the complement fixation test may become positive in extensive forms of the disease.[1, 23] Others consider the skin test to be of little value.[14, 24, 25]

TABLE III. DIAGNOSTIC FINDINGS IN 6 CASES OF PULMONARY BLASTOMYCOSIS TREATED BY RESECTION

CASE	X-RAY	BRONCHOSCOPY	SPUTUM CULTURE FOR FUNGI	PREOPERATIVE DIAGNOSIS
1. J. T.	Density, left apex (inflammatory)	Negative	Negative	Inflammatory disease
2. C. D.	Tumor, left upper lobe	Negative	Negative	Carcinoma
3. J. R. T.	Cyst, left upper lobe	Negative	Negative	Cystic disease
4. J. S.	Density, right upper lobe	Negative	Negative	Inflammatory disease
5. R. J.	Tumor, left upper lobe	Negative	Negative	Carcinoma
6. C. McC.	Cavity, left lower lobe	Negative	Positive for blastomycosis	Blastomycosis

We have established the diagnosis in a case of acute lung abscess by needle aspiration. Such a technique is rarely indicated. Diagnostic thoracotomy will continue to be necessary in some cases of localized, possibly neoplastic, disease, but it is to be hoped that with increasing experience the diagnosis may be established more frequently without operation. In the 20 reported cases of pulmonary resection (Table II) the diagnosis was established prior to operation in only 4 instances. We made a preoperative diagnosis in only 1 of our 6 cases (Table III).

MEDICAL TREATMENT

Cutaneous blastomycosis has responded readily to treatment, whereas systemic lesions have not, until recently, responded regularly to any of a host of agents, including the modern antibiotics. Martin[23] and Smith[1] report benefit from vaccine therapy either alone or followed by iodides. Weisel and Landis[21] are unique in reporting a small series of systemic cases successfully treated by oral and aerosolized iodide therapy.

In 1945 Elson[26] demonstrated the in vitro effectiveness of propamidine against certain fungi including *Blastomyces dermatitidis.* Stilbamidine (4,4′-stilbenedicarboxyamidine) proved to be a more effective diamidine, and in 1951 Schoenbach and his colleagues[27] reported the successful treatment of a case of systemic blastomycosis with this agent. A number of subsequent re-

ports have indicated that stilbamidine is a very effective agent in controlling blastomycosis.[14, 17, 18, 28-33] As yet, however, no large series has been reported and the follow-up periods have been short.

Stilbamidine is a relatively toxic agent.[34] Breakdown products capable of damaging the liver and kidneys develop on exposure to ultraviolet light so that it is imperative that solutions be freshly prepared.[35] The agent is contraindicated in cases of hepatic or renal disease. A number of symptoms may accompany, or shortly follow, the administration of the drug intravenously: hypotension, tachycardia, dizziness, salivation, syncope, incontinence, and the like. A very annoying, but rarely serious, complication is the appearance, several months after therapy, of a fifth cranial neuropathy manifested by paresthesia, hypalgesia, and anesthesia over the region supplied by the trigeminal nerve.

Equally effective against blastomycosis is 2-hydroxystilbamidine. It is more stable in solution and is free of toxic reactions.[13, 14, 33] Snapper and McVay[13] first reported satisfactory response to therapy in 4 cases with severe disease. Large doses of the drug were given over long periods without the appearance of any toxic reaction other than a transient circulatory collapse on one occasion with the very rapid injection of the drug.

As more experience accumulates, it is apparent that these drugs are truly effective agents in blastomycosis, but they will not in all instances control the disease. Smith[33] has completed treatment with stilbamidine or 2-hydroxystilbamidine in 10 cases, and 6 cases are now under therapy or have just completed treatment. His results have been satisfactory. Seabury[14] has treated 12 cases of systemic blastomycosis with these drugs. No serious reactions occurred with 2-hydroxystilbamidine. Seven cases have been treated long enough to be considered well controlled, several as long as two years. Three are now under therapy and are doing well. In two cases treatment failed, and in one case (our Case 6) resection of a residual destroyed lobe was necessary. One failure occurred in a male with a thirty-year history of disease. He died of anoxia two weeks after admission. The second failure was Case L. M., who had a destroyed right upper lobe, two large cavities in the apex of the right lower lobe, and multiple cavities in the upper and lower lobes of the left lung. Sputum conversion occurred under treatment but she relapsed three months after discontinuance of 2-hydroxystilbamidine, and the organisms demonstrated resistance. Murphy[20] has experienced good results in 2 cases but he also has had 2 failures.

Patients are placed on a low-protein, low-purine diet during treatment, because these substances antagonize the action of the drugs. The agents are given in freshly prepared solutions as a slow intravenous drip. Increasing doses of 2-hydroxystilbamidine are given up to 0.225 Gm. in an adult. The drug is given daily or every other day. Treatment may be continuous or in discontinuous series. Seabury[14] advises 5 to 8 Gm. for moderately extensive pulmonary disease, and 8 Gm. or more for cases with large areas of necrosis

or abscess formation. The drugs are stored for as long as a year in numerous tissues in the body[36] and it is possible that the therapeutic effect is prolonged.

Longer follow-up periods and more experience will be needed to evaluate the effectiveness of treatment and to determine the best treatment regimens. Experience to date is sufficient to indicate their use in any visceral or serious cutaneous form of the disease. Unfortunately the drugs are expensive. Stilbamidine isethionate* has been available on prescription for some time; 2-hydroxystilbamidine isethionate* is now being released for general use.

SURGICAL TREATMENT

Pulmonary blastomycosis usually occurs as a diffuse lesion not amenable to surgical therapy, but sometimes the lesion is localized and excisional therapy has appeared rational. We have been able to collect 20 reported cases of pulmonary resection for blastomycosis (Table II). Two of Smith's[1] cases, J. T. and C. D., are excluded from the reported series as they are included in our personal series. The bulk of the surgical experience with pulmonary blastomycosis antedates effective chemotherapy. In the majority of cases no effective fungistatic agent was available even after operation.

No follow-up is available in 2 cases, and 3 patients died in the immediate postoperative period. Four cases died of dissemination of the disease from six days to two years after resection. Five patients developed signs of active disease following surgery but responded to medical treatment and the disease was arrested. This treatment included human serum, blastomycin, iodides, undecylenic acid, stilbamidine, and 2-hydroxystilbamidine. In 7 cases the disease was apparently controlled by pulmonary resection alone, although blastomycin was used in one case. Murphy[20] reports a postoperative recurrence following lobectomy which has not responded to vigorous treatment with iodides, undecylenic acid, and stilbamidine.

Our experience with pulmonary resection in 6 cases of blastomycosis is briefly outlined.

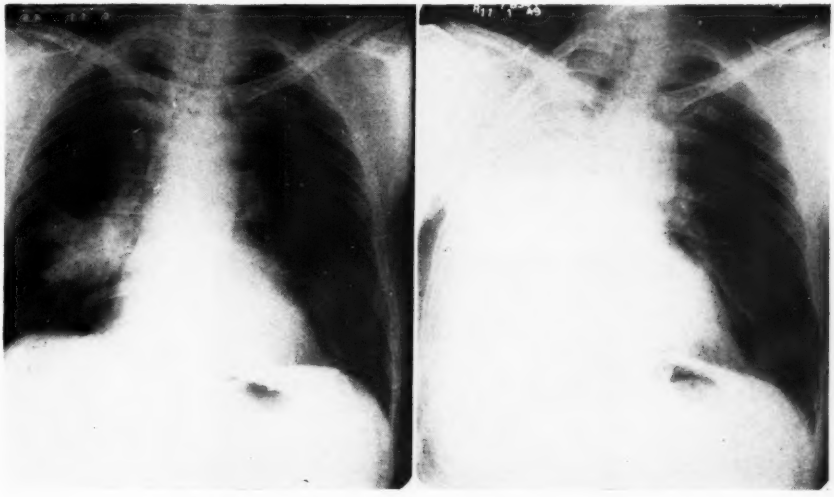
CASE 1.—J. T., a 39-year-old white housewife from Tennessee, was admitted Aug. 10, 1947, with pain in the left anterior chest, fatigue, weakness, a daily fever of 102° F., and an 11 pound weight loss during the previous eight weeks. No cough or hemoptysis had occurred. On examination fine râles and decreased breath sounds were noted in the left apex. A therapeutic pneumothorax had been induced two weeks prior to admission. Laboratory studies were not remarkable. Sputum smears and cultures were repeatedly negative for tubercle bacilli and pathogenic fungi. A roentgen film exhibited a homogeneous density in the medial portion of the left apex. These changes had been absent in a film taken six months before. Unfortunately, the films were lost. Bronchoscopic examination was negative. On Sept. 4, 1947, a left pneumonectomy was performed for a lesion in the left upper lobe, very firmly adherent to the parietal pleura, which was thought to be a carcinoma. Numerous organisms resembling *Blastomyces dermatitidis* were observed on tissue examination. Organisms were later cultured from a chest wall lesion. The skin test and complement fixation tests were negative. Iodide therapy was begun. Two weeks following operation a metastatic lesion destroying the left seventh rib was noted. The rib was resected and the area radiated with 900 r. in 6 doses. A sinus tract persisted and skin nodules appeared the following year. Intercostal nerves were severed

*The William S. Merrel Co., Cincinnati 15, Ohio.

for severe intercostal neuralgia. A second costectomy was performed elsewhere. On June 23, 1950, while undergoing a posterior rhizotomy for persistent pain, she developed cardiac arrest and died.

Comment.—Surgical therapy failed in this case because of systemic spread of the disease which occurred concurrently with operation.

CASE 2.—C. D., a 62-year-old white businessman from Alabama, was admitted June 15, 1948, complaining of cough, hemoptysis, afternoon temperature of 102° F., easy fatigue, and a 20 pound weight loss. Physical examination revealed râles and dullness posteriorly and laterally in the right lower chest. The sedimentation rate was elevated. The hemogram was not remarkable. Sputum examinations were repeatedly negative for all pathogenic fungi. Roentgenography revealed a shadow in the dorsal segment of the right lower lobe, suggesting an abscess associated with tumor (Fig. 1, *A*). Bronchoscopy was negative. Skin test and complement fixation studies were negative postoperatively. On June 26, 1948, a right pneumonectomy was performed for a suspected carcinoma. Smear, tissue sections, and cultures all demonstrated *Blastomyces dermatitidis.* Occasional hemoptysis



A. *B.*

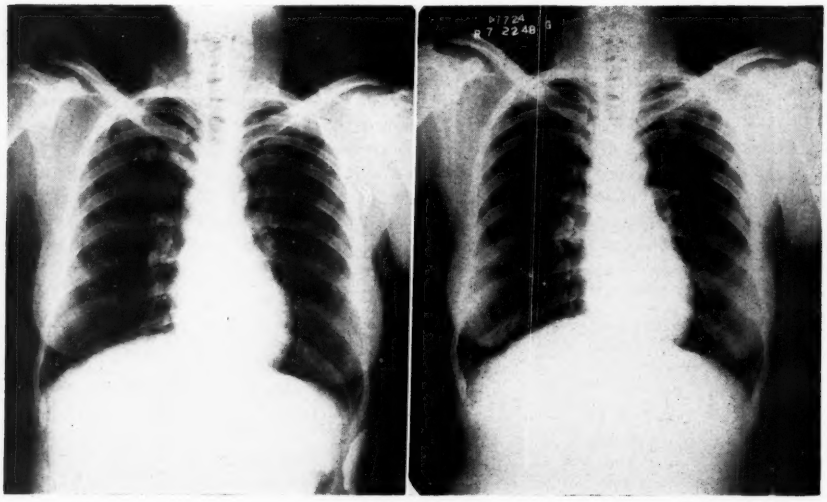
Fig. 1.—Case 2. C. D. *A*, Preoperative roentgenogram; *B*, roentgenogram seventeen months after right pneumonectomy.

occurred for one year following operation. One postoperative sputum smear revealed fungi thought to be blastomycetes, but repeated cultures of sputum and bronchial washings were negative. The bronchial stump appeared normal at bronchoscopy. There was never clinical or roentgenographic evidence of disease in the remaining lung (Fig. 1, *B*). He was treated with a vaccine, and with iodides for two years postoperatively. At the age of 68 this gentleman is apparently well, five years and nine months after operation.

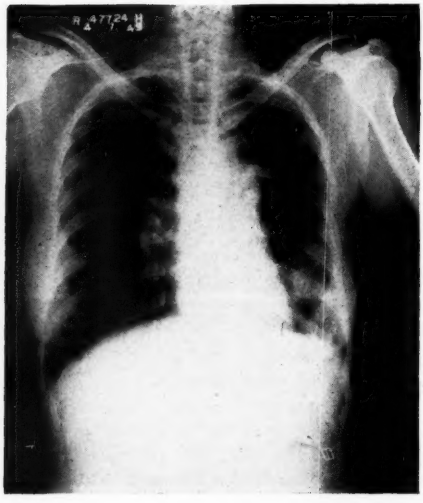
Comment.—The final result is excellent in this case though there may have been postoperative activity. A more conservative operation might have sufficed had the diagnosis been established prior to operation.

CASE 3.—J. R. T., a 36-year-old housewife from Alabama, was first admitted June 17, 1946, with a two-month history of cough and hemoptysis. There were no other related symptoms. Routine laboratory studies were negative. Roentgenography revealed a thin-walled "cyst" in the left apex with no inflammatory reaction around it (Fig. 2, *A*).

Bronchoscopy was negative. On this admission, surgery was performed for an unrelated condition. She was readmitted on Jan. 22, 1948, complaining of blood-streaked sputum, frank hemoptysis of 3 ounces of blood on two occasions six weeks apart. There were no



A. *B.*

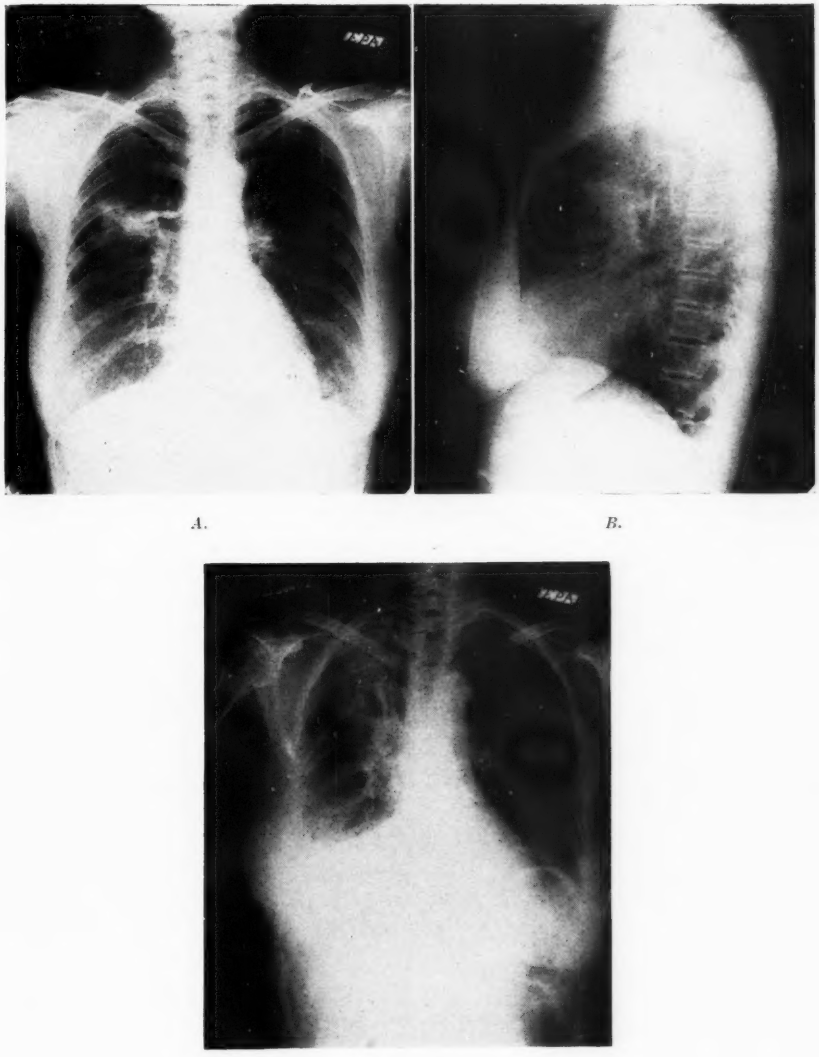


C.

Fig. 2.—Case 3. J. R. T. *A*, Roentgenogram, June, 1946; *B*, roentgenogram, January, 1948; *C*, roentgenogram eight months following left upper lobectomy.

other symptoms. Physical findings were not remarkable. Roentgenography revealed a multilocular cavity in the left apex four times the size of the cavity seen two years previously (Fig. 2, *B*). The skin test and repeated sputum studies were negative for blasto-

mycosis. On Aug. 2, 1948, a left upper lobectomy was performed. The upper lobe was densely adherent to the parietal pleura and it contained a 1.5 by 2.0 cm. cavity. Smear, tissue sections, and culture revealed *Blastomyces dermatitidis*. Iodides were given em-



A. *B.*

C.

Fig. 3.—Case 4. J. S. *A* and *B*, Roentgenograms reveal an irregular shadow near the hilum in the right upper lobe. Diffuse infiltration of both lungs with partial contraction of left lower lobe; *C*, Roentgenogram on the eighth day following right upper lobectomy.

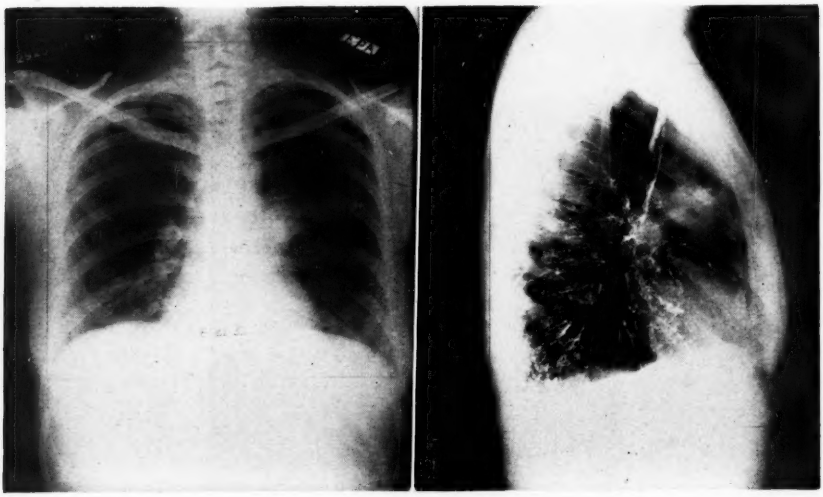
pirically for a period of two years. The patient is alive and well five years and six months following operation. Repeated roentgenograms have shown no evidence of disease (Fig. 2, *C*).

Comment.—A persistent cavitary lesion due to blastomycosis was apparently cured by lobectomy.

CASE 4.—J. S., a 55-year-old white housewife from Mississippi, was admitted on June 6, 1952, with a three months' history of chills, fever to 101° F. daily, cough, and malaise. The patient also had angina pectoris and required as many as 100 nitroglycerin tablets per week. Physical examination was not revealing. Roentgenography revealed an irregular shadow adjacent to the right hilum and located in the anterior portion of the right upper lobe (Fig. 3, *A* and *B*). Bronchoscopy was negative. Sputum smears were negative for fungi, and cultures were later reported as negative. Hemogram was normal. The electrocardiogram showed definite evidence of myocardial disease. On June 13, 1952, a right upper lobectomy was performed for a hard granulomatous lesion. Tissue sections and cultures of hilar lymph nodes were positive for *Blastomyces dermatitidis.* The postoperative course was uneventful and the patient appeared to be free of pulmonary disease (Fig. 3, *C*). She died suddenly at home, five months later, of coronary thrombosis.

Comment.—The blastomycosis appeared to be controlled in this case until the time of her death from a myocardial infarction.

CASE 5.—R. W. J., a 37-year-old white housewife from Mississippi, admitted Aug. 20, 1952, with cough, hemoptysis, low-grade fever, malaise, left anterior chest pain, and a 24 pound weight loss during a two-month period. She had experienced attacks of dyspnea and palpitation, without hypertension, occurring at one- to two-month intervals for three years. Roentgenography revealed a large circumscribed lesion in the anterior segment of the left upper lobe (Fig. 4, *A* and *B*). The hemogram was normal. Sputum smears and,



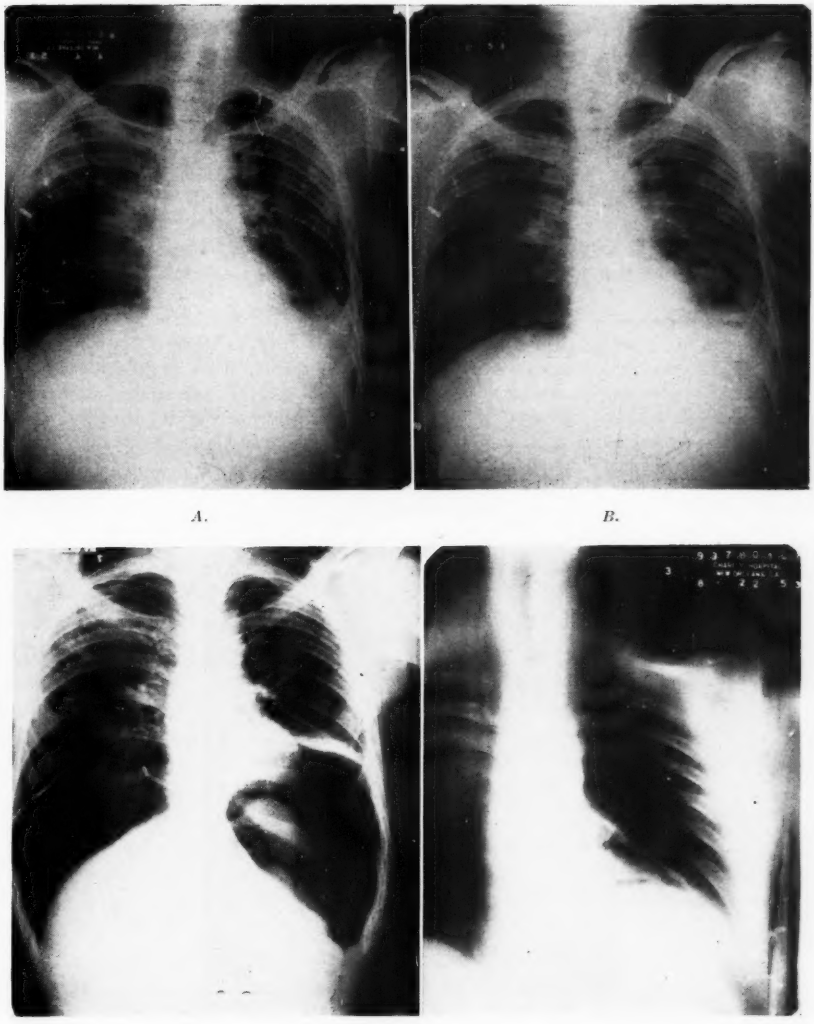
A. *B.*

Fig. 4.—Case 5. R. W. J. *A* and *B*, Roentgenograms revealing circumscribed lesion in anterior segment of left lower lobe.

later, cultures were negative for fungi. A bronchoscopy was negative. On bronchography the left upper lobe bronchus could not be filled with dye (Fig. 4, *B*). On Aug. 29, 1952, a left upper lobectomy was performed for a firm 6 by 5 cm. granuloma in the anterior segment. The patient developed a severe sinus tachycardia on the operating table. She did not recover from this and died three hours following operation. Smears, tissue sections, and cultures revealed *Blastomyces dermatitidis.* Post-mortem examination revealed a pheochromocytoma of the left adrenal.

Comment.—This is a most regrettable fatality due to an unsuspected pheochromocytoma.

CASE 6.—C. McC., a 41-year-old Negro laborer from Louisiana, was admitted to the Charity Hospital on March 28, 1953, with a history of onset of cough and high fever ten



A. *B.*

C. *D.*

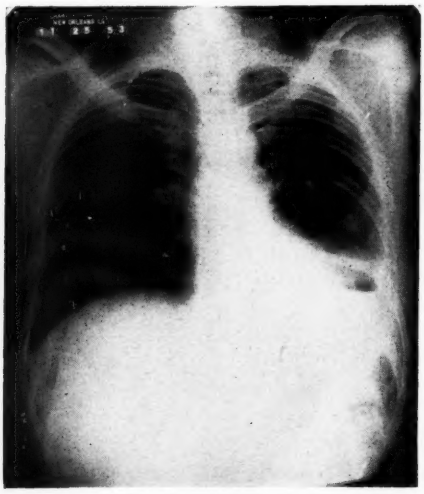
Fig. 5.—Case 6. C. McC. Roentgenograms demonstrating changes following therapy. *A*, April 4, 1953, prior to treatment; *B*, May 12, 1953, after 3.75 Gm. of 2-hydroxystilbamidine; considerable clarity of exudate; *C*, July 13, 1953, appearance after 7.5 Gm. of 2-hydroxystilbamidine pneumoperitoneum; *D*, Aug. 22, 1953, planogram demonstrating complete contraction of left lower lobe with cavitation.

months before. The symptoms did not subside on six weeks' therapy with various antibiotics. The fever gradually declined, but cough and 100 c.c. of yellow sputum daily persisted. Four months prior to admission he developed fever again, and a month later an

indurated ulcer of the left cheek appeared and persisted. Biopsy of the ulcer revealed *Blastomyces dermatitidis* on tissue section and on culture. The patient was almost totally blind from cataracts. On physical examination a 3 cm. shallow ulcer was present on the left cheek. Moist râles were present over both lung fields. Routine laboratory studies were normal. Roentgenography revealed bilateral infiltration involving principally the upper half of the lung fields, patchy but firm in appearance (Fig. 5, *A*). The apices were not involved. The sputum was repeatedly positive on smear and culture for blastomycetes.

Medical treatment was directed by Dr. John Seabury. On April 11, 1953, he was started on 250 mg. of 2-hydroxystilbamidine intravenously daily for three days and then every other day until May 8, 1953 (Fig. 5, *B*). A total of 3.75 Gm. was given. The ulcer of the cheek healed rapidly. Pneumoperitoneum was commenced in an effort to collapse cavities in the right mid-lung and the left lower lobe. A second course of 3.75 Gm. of the drug was commenced on May 24, 1953, with 15 doses of 250 mg. given intravenously every other day (Fig. 5, *C*). By Aug. 22, 1953, the right lung and the left upper lobe had cleared considerably but the left lower lobe became progressively atelectatic and planograms demonstrated honeycombing and one large area of cavitation (Fig. 5, *D*). A severe hacking cough persisted.

The patient received a third course of 2-hydroxystilbamidine, 225 mg. daily for seven days prior to operation and for five days postoperatively. On Sept. 18, 1953, a left lower lobectomy was performed. Because of dense adhesions the resection was technically very difficult. The lobe was almost completely replaced by fibrous tissue and contained one large multiloculated cavity measuring 5 by 4 cm. No culture was made of the lung. Since operation the patient has been free of all symptoms referable to blastomycosis, and sputum cultures have been repeatedly negative for blastomycetes (Fig. 5, *E*).



E.

Fig. 5.—*E*, Nov. 25, 1953, two months after left lower lobectomy and total of 10.2 Gm. of 2-hydroxystilbamidine.

Comment.—The management of this case, we feel, approaches the ideal. The diagnosis was established and vigorous specific therapy was administered. In spite of extensive bilateral disease, sputum conversion and clearing of the roentgen shadows occurred, but with evidence of residual complete destruction and cavitation of the left lower lobe. Lobectomy removed the destroyed tissue and relieved the patient of his residual symptoms.

In summary, we have performed 2 pneumonectomies and 4 lobectomies for pulmonary blastomycosis. The diagnosis was established prior to operation in only 1 case. In 2 cases bronchogenic carcinoma was suspected, in 2 cases an inflammatory lesion, and in 1 case a persistent cavity of undetermined etiology was present. Three patients died: one immediately following surgery from a sustained tachycardia incident to a pheochromocytoma; and a second three years after resection during an operation to relieve pain incident to her recurrent disease. The third patient, apparently free of blastomycosis, died of a myocardial infarction six months after operation. Three patients are alive and well 9 months, 66 months, and 69 months, respectively, after resection. This last patient may have had postoperative activity of his disease the first year after operation.

DISCUSSION

It seems inescapable that the diagnosis of blastomycosis is frequently missed both clinically and at autopsy. The organisms are difficult to recognize in exudates and in tissues and the pathologic lesions are not diagnostic. Whenever diagnostic suspicion has increased, the incidence of the disease in the locality has arisen. It is quite likely that a number of self-limited, unrecognized cases have occurred. It is our experience that even when the disease is suspected, diagnosis is sometimes difficult, and we have failed to recover organisms on repeated examination and culture of sputum in cases with active disease.

The best chemotherapeutic agent known is 2-hydroxystilbamidine, because of its effectiveness and freedom from toxicity. It will usually, but not always, cause a regression of the pathologic lesions with closure of cavities.[14] It will usually cause the sputum to revert to negative and will alleviate the clinical manifestations of the disease.

Blastomycosis, contrary to many published pathologic studies, may cause extensive destruction of pulmonary tissue with abscess and cavity formation. It is to be expected, as several authors have suggested,[17, 25, 31, 32] that in some instances surgical excision of residual cavities and destroyed tissues will be indicated following chemotherapy. Certainly such was true in our Case 6, and would probably have been true of the cavitary lesion in our Case 3. Only further experience will indicate how frequently planned surgical excision will be necessary following chemotherapy.

Smith[33] has had no occasion to recommend excision in his experience with 16 cases. Our Case 6 represents one indication for resection in 12 cases treated by Seabury. In some cases recently under treatment it is too early to decide whether resection will be indicated. In his case L. M., lung destruction was so general that resection was out of the question. Hughes[40] has two cases under observation following stilbamidine therapy which, he feels, should apparently have the residual lesions resected.

The parallelism between the management of pulmonary tuberculosis and pulmonary blastomycosis is apparent. Both represent phases of a systemic infection. Effective chemotherapy is available for both. In both conditions surgical excision is helpful in the removal of destroyed tissue and residual lesions following medical treatment.

It is highly desirable that the diagnosis be made prior to operation. With effective chemotherapy operation may be obviated, but if required will be

much safer. Diagnostic thoracotomy may still be occasionally required and if the diagnosis is made only after resection a postoperative course of 2-hydroxystilbamidine is indicated. The amount of drug that should be used depends on the character of the lesions present. If resection is impossible, diagnostic biopsy is valuable as it will enable specific chemotherapy. Resection may be possible later if required.

CONCLUSIONS

1. Pulmonary blastomycosis is not uncommon in some localities in North America. An increased "incidence" of the disease commonly follows greater clinical suspicion coupled with vigorous diagnostic efforts.

2. On the basis of three years' experience 2-hydroxystilbamidine appears to be an effective, nontoxic therapeutic agent for blastomycosis.

3. In some cases of pulmonary blastomycosis lung resection is required following control of the active disease by diamidine therapy. One such case is reported.

4. Pulmonary resection, or biopsy, in unsuspected cases of pulmonary blastomycosis is hazardous and should be promptly followed by vigorous diamidine therapy. Every effort should be made to establish the correct diagnosis, and to administer 2-hydroxystilbamidine, prior to operation.

5. On the basis of relatively short-term observations the prognosis of pulmonary blastomycosis is excellent when treated with 2-hydroxystilbamidine followed by surgical resection if necessary.

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DISCUSSION

DR. M. M. NEWMAN, St. Albans, N. Y.—We have had the opportunity of treating two cases of advanced coccidioidomycosis at St. Albans in collaboration with Dr. I. Snapper of New York City.

(Slide.) This is a 24-year-old white male who had a wedge resection of a granuloma of the right upper lobe at another hospital. This was followed by empyema and decortication was done at that hospital. The lung failed to re-expand. He had fever, anorexia, and a weight loss of 20 pounds. He was then transferred to our hospital. The empyema was draining through six sinuses in the chest wall. Coccidioidin No. 1 was positive; complement fixation test was positive at 1 to 64.

(Slide.) This shows the original coin lesion in the posterior segment of the right upper lobe, and here the empyema after resection.

(Slide.) He received supportive care, after which another decortication of the right lung was done on June 16, 1952. About three weeks after operation he developed headache and fever. Lumbar puncture showed turbid fluid, from which *C. immitis* could be cultured. He was transferred to Mt. Sinai Hospital. There he received 23 Gm. of 2-hydroxystilbamidine from July 28, 1952, to Nov. 5, 1952. There was complete disappearance of meningeal signs. He gained 30 pounds and had no residual neurologic disability. This man now drives a large tank truck between cities in northern New York.

(Slide.) This was a 28-year-old white male who was stationed at an Air Force base in Arizona. Between August, 1950, and August, 1952, he had five spontaneous pneumothoraces. In July, 1952, he had a right spontaneous pneumothorax. The lung failed to re-expand on suction and a cavity was seen in the right upper lobe. PPD No. 1 was positive, coccidioidin No. 2 was doubtful. In October, decortication of the right lung and resection of the posterior segment of the right upper lobe was done, under the impression that this was tuberculosis. Postoperatively there was a fistula and empyema. In December he had a second decortication and culture of the specimen showed *Coccidioides immitis.*

(Slide.) The lung collapsed again. Coccidioidin skin test had become strongly positive; complement fixation was positive at 1:80. A nine-rib thoracoplasty was done to control the empyema. Between December, 1952, and August, 1953, he received 8 Gm. of 2-hydroxystilbamidine with no apparent change. Between August and October, 1953, he received another 8 Gm. Three of six gastric cultures in November, 1953, were positive for *C. immitis.* In December he received a new drug, 2-aminostilbamidine, and since then has had seven consecutive negative cultures.

We feel we are in a new era in treatment of the deep mycoses.

DR. FELIX A. HUGHES, JR., Memphis, Tenn.—Stilbamidine and 2-hdyroxystilbamidine have been used for blastomycosis at Kennedy Hospital by Dr. Sutliff, Chief of the Infectious Diseases Section. In April of this year, Dr. Sutliff, Dr. Kyle, and Dr. Hobson reported the results of the treatment of 25 cases of blastomycosis in Memphis to the American College of Physicians, and Dr. Sutliff kindly allowed me to review the paper, and some of my remarks are based on this paper. Seventeen of these cases were at Kennedy, eight were at other hospitals in Memphis. The mortality in these cases has been 8 per cent, with a total mortality of 20 per cent. Eight per cent is in contrast to 35 per cent in the series of Smith and associates and 78 per cent in the series of Martin and co-workers.

The prognosis apparently has been greatly improved. Before the advent of the aromatic diamidines, 11 cases were treated; 5 of these were arrested, 3 by surgery, 2 by pulmonary resection, and 1 by excision of a skin lesion. These surgical excisions gave the only immediate cures in this group. Stilbamidine was used in the treatment of 7 cases; one of these has a persistent pulmonary lesion that apparently should be resected. In 12 cases 2-hydroxystilbamidine was used, with 7 arrested, but 2 have persistent pulmonary lesions. In all, 3 cases have persistent pulmonary lesions that we think should probably be removed. At the present time our inclination would be to give hydroxystilbamidine to the known cases of blastomycosis with a solitary pulmonary lesion, as the initial treatment. The case could then be followed by planograms and cultures, so that an active and/or persistent pulmonary lesion could be removed.

There are other reasons to indicate that surgery might be useful. One is the unpredictability of this disease in that it tends to recur after being apparently cured. The other is that in the two cases we have resected even without the use of these drugs the patients have remained well.

DR. O. THERON CLAGETT, Rochester, Minn.—I suspect very strongly that blastomycosis is just about as common as pulmonary histoplasmosis and coccidioidomycosis, and I think these infections are all very similar in many respects. It is time to recognize the fact that mild pulmonary infections with these fungi occur and heal spontaneously rather commonly. However, severe and complicated varieties such as have been presented here also may occur. I do not want to minimize the importance of the advance that stilbamidine

therapy of blastomycosis represents, but I do think we have to recognize that there is a very strong natural tendency for blastomycosis to heal spontaneously, and that an accurate estimate of the efficacy of stilbamidine in the treatment of blastomycosis will require greater experience.

Recently, Dr. Kunkel, Dr. Weed, Dr. McDonald, and I reviewed 90 cases of blastomycosis that have been seen at the Mayo Clinic. In 54 the lesion was primarily cutaneous, in 36 it was systemic. Of the 36 systemic infections, 10 were treated by surgery and iodides, and healing occurred even though the infection involved lung, bones, neurologic system, and genitourinary system. In our experience, the treatment of blastomycosis with stilbamidine has not been uniformly successful. Our surgical experience with pulmonary blastomycosis consists of five patients in whom pulmonary resection was carried out. All are alive; four of them are well, one developed blastomycosis of the contralateral chest wall subsequent to the pulmonary resection. As an indication of the chronicity of blastomycosis and the difficulty in knowing when it is actually healed, one case in our experience had cutaneous blastomycosis thirty-two years previous to pulmonary resection for pulmonary blastomycosis.

DR. WILL C. SEALY, Durham, N. C.—We have had an extensive experience with blastomycosis at Duke Hospital; it seems that there are a great many cases in the eastern part of our state. I would like to say one word about the diagnosis. In our last 12 cases we have not done surgery because the diagnosis has been made clinically. They have been treated with drugs and have not required operation. The last three cases have been children, and by getting tracheal aspirations the organisms were demonstrated on smears. The skin test for blastomycosis is sometimes of considerable importance. If it is positive, with a pulmonary lesion, I think one should be more than suspicious of blastomycosis and do further and more detailed studies. Of course if it is negative, it does not rule out blastomycosis.

The fifth nerve neuropathy, with treatment with stilbamidine, occurs very frequently, sometimes as long as six months after treatment, and it does not occur until the patient is exposed to sunlight. We had one patient with blastomycosis of the trachea who developed neuropathy six months later. The operation was done in the winter and he was not exposed to the sun until summer and then developed trigeminal neuropathy. Our neurosurgeons have used this in treating tic douloureux. I might say this complication also occurs with 2-hydroxystilbamidine, for in one patient with extensive coccidioidomycosis treated with this, there was development of trigeminal neuropathy just as with stilbamidine, so I suspect that some of the other reports of lack of toxicity may be due to the fact that the patient was not exposed to ultraviolet radiation.

DR. ACREE (Closing).—I should like to thank our discussers very much. We recognize that a limited time has passed since these new drugs have come forward and we are viewing them with hopefulness but are also wondering what is going to happen in time. We realize that in some patients the preoperative diagnosis is extremely difficult to make. When an individual has been operated upon and the diagnosis of blastomycosis has been made, we feel that he should receive postoperative treatment with 2-hydroxystilbamidine, for, as we have shown, the danger of dissemination is great.

THORACOPLASTY

A New Osteoplastic Technique

Viking Olov Björk, M.D.
Stockholm, Sweden

PARTIAL thoracoplasty with extrafascial apicolysis, according to Semb,[1] has proved to be a valuable procedure which we will continue to use in selected cases. After a personal experience of more than 300 first-stage operations, according to Semb, a new technique has gradually been developed in order to overcome the disadvantages inherent in rib resection with apicolysis.

These disadvantages encountered are:

1. In the immediate postoperative period the unstable chest wall after the rib resection will considerably alter the normal physiology of respiration[2]:

   A. The paradoxical movements of the lung will impair the alveolar ventilation.

   B. The unstable chest wall will impair an effective cough mechanism and increase the incidence of atelectasis.

   C. Accumulation of fluid in the apicolysis space may produce a considerable compression atelectasis of the lung. In the atelectatic part of the lung the blood will pass nonventilated alveoli and return unsaturated to the left atrium. A decreased arterial oxygen tension will result for a period of several weeks.[2]

2. During the first year after the operation there is some re-expansion of the lung, which in many cases will result in the reopening of a cavity.

Attempts to overcome these disadvantages have been made along the following lines:

I. The apicolysis space has been filled with plastic material. This has then to be removed after some weeks at a second stage, or it is left in place. The plastic plomb may, however, become infected after some months or years. If then a bronchial fistula is found, extensive resection of the chest wall and lung tissue has to be done.[3]

II. Holst has described several improvements.[4] The ribs are divided anteriorly and posteriorly and sutured down under a rib, usually the fifth,

From Sabbatsberg Hospital, Surgeon-in-chief: C. Crafoord, M.D., Professor; St. Göran Hospital, Physician-in-chief: A. Westergren, M.D., Professor; Söderby Hospital, Physician-in-chief: T. Bruce, M.D.

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left in place, but stripped from the periosteum. The first rib was left intact and an extrapleural apicolysis was performed. A fixation of the apical pleura was performed. A thin pleura, however, is considered a contraindication to this procedure.

III. Extrafascial air refills have been performed but not found worth while. The apex of the lung is found on approximately the same level whether air refills have been given or not.[5]

THE AUTHOR'S TECHNIQUE

General Principles.—

A new roof of the thorax is obtained by resection of posterior portions of the ribs in increasing lengths from above and downward. The ribs are then bent in the costal cartilages and fixed to the posterior end of the uppermost intact rib by stainless steel sutures through drill holes. An extrapleural apicolysis to the aortic arch or the azygos vein is performed. The first rib is divided both anteriorly and posteriorly and fixed to the transverse process of the fifth or sixth rib. The first rib will then prevent the lung from re-expanding above the new dome. Thus the two disadvantages with modern thoracoplasty have been overcome:

1. A stable chest wall has been obtained.
2. The lung is prevented from re-expanding above the new roof.

When the thoracoplasty is used in combination with resection, the first rib may be left in place. Then the second rib must be fixed as close to the mediastinum as possible. A repair of the mediastinal pleura to the first intercostal muscle bundle is also necessary. With this modification a stable chest is obtained. Even with a very thin pleura, only a negligible re-expansion of the lung may be found.

Details of the Surgical Procedure.—

First Step. Incision.—A paravertebral incision is made and continued anteriorly at least 5 cm. below the tip of the scapula. In a case where resection and thoracoplasty is performed, the incision is carried forward along the lower border of the fifth or sixth rib. The paravertebral part of incision is placed about 3 cm. from the midline. The posterior flap is undercut as far as the midline to permit division of the trapezius and the rhomboid muscles as near as possible to the spinous processes.[6, 7]

Second Step. Elevation of Scapula and Preparation of Resection Area.— The thoracic dome is exposed and the scalenus posterior, medius and anterior as well as the serratus anterior to the first and second rib are divided well above the attachment to the periosteum to avoid impairment of the nutrition to the ribs.

Third Step. Rib Resection.—The posterior ends of, usually, the upper five ribs, sometimes the upper six, and occasionally the upper seven are resected (Fig. 1). The most commonly used five-rib thoracoplasty will be described. The ribs are divided posteriorly at the tip of the transverse processes, which are always left intact. Roughly a little more than 5 finger-

breadths of the fifth rib, 4 fingerbreadths of the fourth rib, 3 fingerbreadths of the third rib, 2 fingerbreadths of the second rib, and 1 fingerbreadth of the first rib are resected. Before the ribs are fixed they are bent down to the intended position to ascertain their optimal length and position. Sometimes

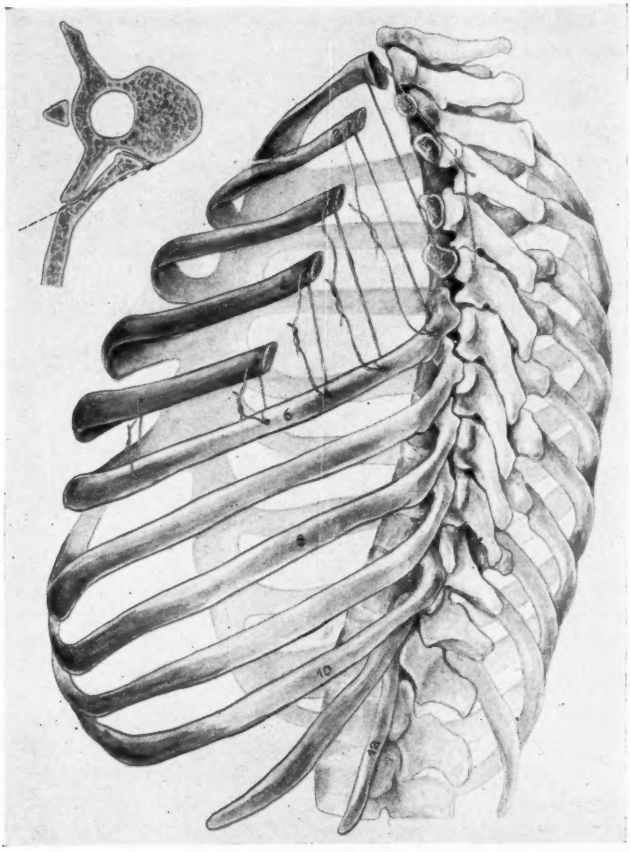


Fig. 1.—The posterior ends of the upper five ribs are resected in increasing lengths.

more of the ribs, usually of the fifth and first, has to be resected. It is important to resect enough of the first rib to have it as straight as possible (Fig. 2) and fix it as close to the mediastinum as possible. Otherwise the lung may expand through the aperture medial to the first rib (Fig. 3). The periosteum is stripped away from the upper border of the posterior end of the sixth rib.

Fourth Step. Apicolysis.—The upper four intercostal bundles are divided. Then an extrapleural strip starts above the first rib. If the pleura is thin, the apicolysis is performed in the extrafascial plane. The posterior cut end

of the first rib is pulled downward with the Semb rib forceps, when remaining attachment of scalenus medius and anticus are cut with scissors (Fig. 4). The subclavian vein is gently detached from the first rib and the posterior

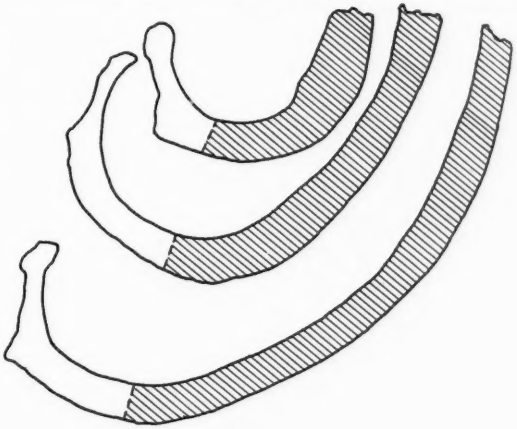


Fig. 2.

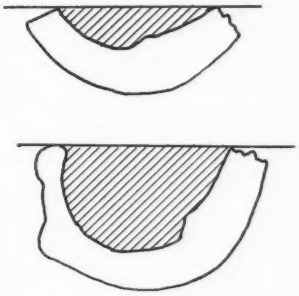


Fig. 3.

Fig. 2.—Enough of the first and second rib must be resected in order to have the remaining portion of the rib as straight as possible.

Fig. 3.—If too short a segment of the first rib is resected, there will be an aperture medial to the rib with re-expansion of the lung (lower diagram). When more of the first rib is resected, it can be fixed closer to the mediastinum (upper diagram).

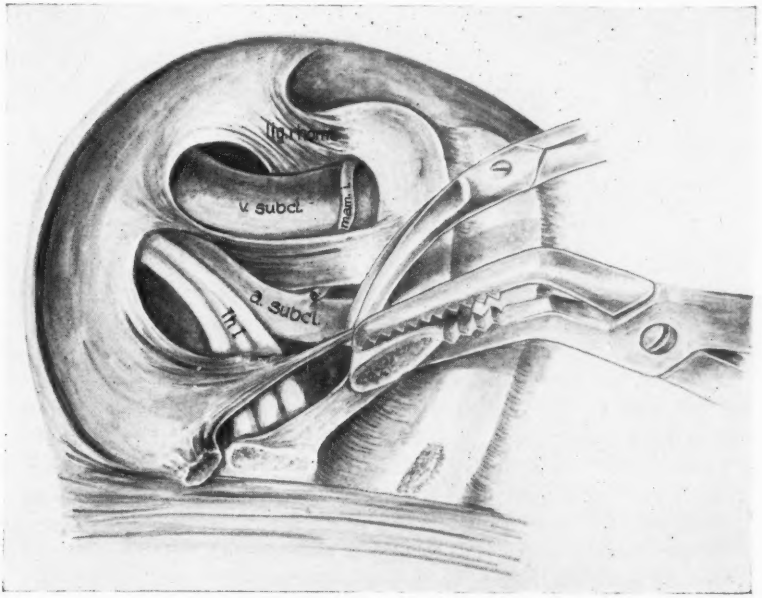
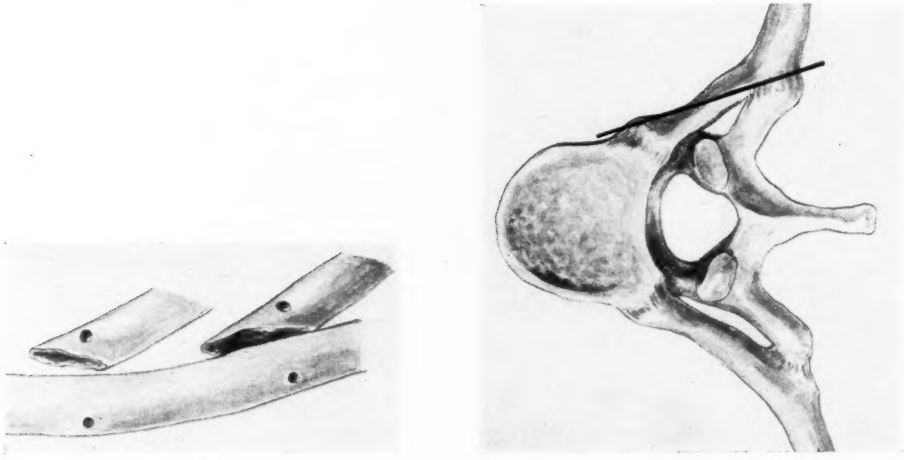


Fig. 4.—The posterior cut end of the first rib is pulled downward when the remaining attachment of scalenus medius and anticus are cut with scissors. The subclavian vein is detached from the first rib and the costo clavicular (rhomboid) ligament, which is divided. The first costal cartilage is then divided anteriorly to the internal mammary artery (right-sided thoracoplasty).

aspect of the costoclavicular (rhomboid) ligament, which is divided with scissors. The first rib may now be pulled more downward and outward when the medial aspect of the first costal cartilage anteriorly to the internal mammary artery is gently dissected, avoiding damage to this artery and the pleura. The first costal cartilage is cut as close to the sternum as possible, and the perichondrium is divided anteriorly. Now it is easy to bend the ribs downward and carry the apicolysis down to the aortic arch on the left side or to the azygos vein on the right side. If the pleura is inadvertently opened, a tube is immediately inserted intrapleurally for continuous suction.



A. *B.*

Fig. 5.—*A*, The holes are placed close to the upper border of the resected ribs and close to the lower border of the sixth rib. This will prevent the sutures from cutting through the ribs. *B*, For the first rib a hole is drilled through the transverse process and the remaining portion of the fifth or sixth rib.

Fifth Step. Fixation.—Small drill holes are made in the posterior ends of the divided ribs. These holes are placed as close to the upper border of the rib as possible. Corresponding holes are then made in the lower border of the sixth rib (Fig. 5, *A*). This will prevent the sutures from cutting through the ribs. For the second rib a hole is drilled in the sixth rib medial to the transverse process. For the first rib a hole is drilled through the transverse process and the remaining portion of the fifth or sixth rib (Fig. 5, *B*). In the most posterior holes an ordinary drill bore is used, a spoon being placed inside the chest to prevent injury to the lung. To make the other holes, I use an especially designed drill bore (see Fig. 6), manufactured by Stille, Sweden, modified from Brock. Stainless steel sutures of 0.8 mm. diameter are threaded through the holes. If these are difficult to find, a wide-bore needle is passed through the hole and the steel thread inserted into the needle. Finer stainless steel sutures and wires have been found to break too easily. The ribs are then bent in the

cartilages. The sutures are drawn taut and tied when a stable roof of the chest is obtained (Fig. 7). A fixation of the mediastinal pleura to the first rib is then performed (Fig. 8).

A drainage tube is always left in the apicolysis space and intermittently opened to drain off the accumulated fluid. As the roof of the chest is stable, the accumulated fluid will not compress the lung as in an ordinary thoracoplasty, but instead the air in the apicolysis space is forced by the fluid into the tissues, producing a subcutaneous emphysema. The tube is left in twenty-four to forty-eight hours only.

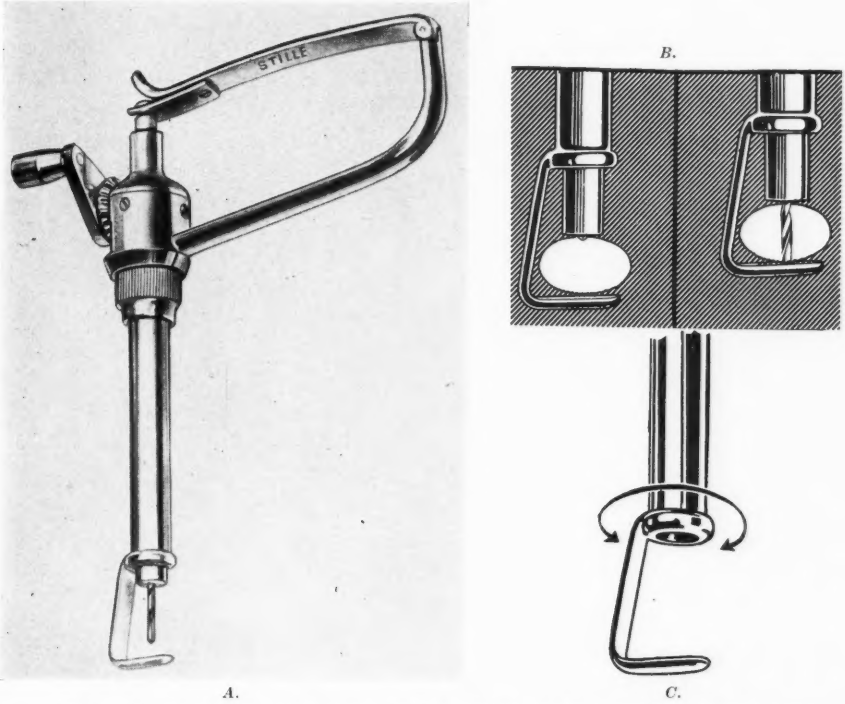


Fig. 6.—*A*, To make the holes in the ribs a specially designed drill bore is used (manufactured by Stille, Sweden). *B*, This bore does not slip off the rib and the lung is protected. *C*, It can be turned in any direction without changing the grip of the hand.

Details of Surgical Procedure If the Thoracoplasty Is Used Simultaneously With Resection.—

First Step. Incision as Above.—The thorax is opened after resection of the posterior part of the fifth or sixth rib. The periosteum is then stripped from the lower border of the rib and the chest is entered through this periosteum under the rib as recommended by Brock. After completion of the resection either the above-mentioned steps for thoracoplasty are followed or the following modification is made:

Second Step.—The thoracic dome is exposed, the muscles inserting on the first rib being left intact.

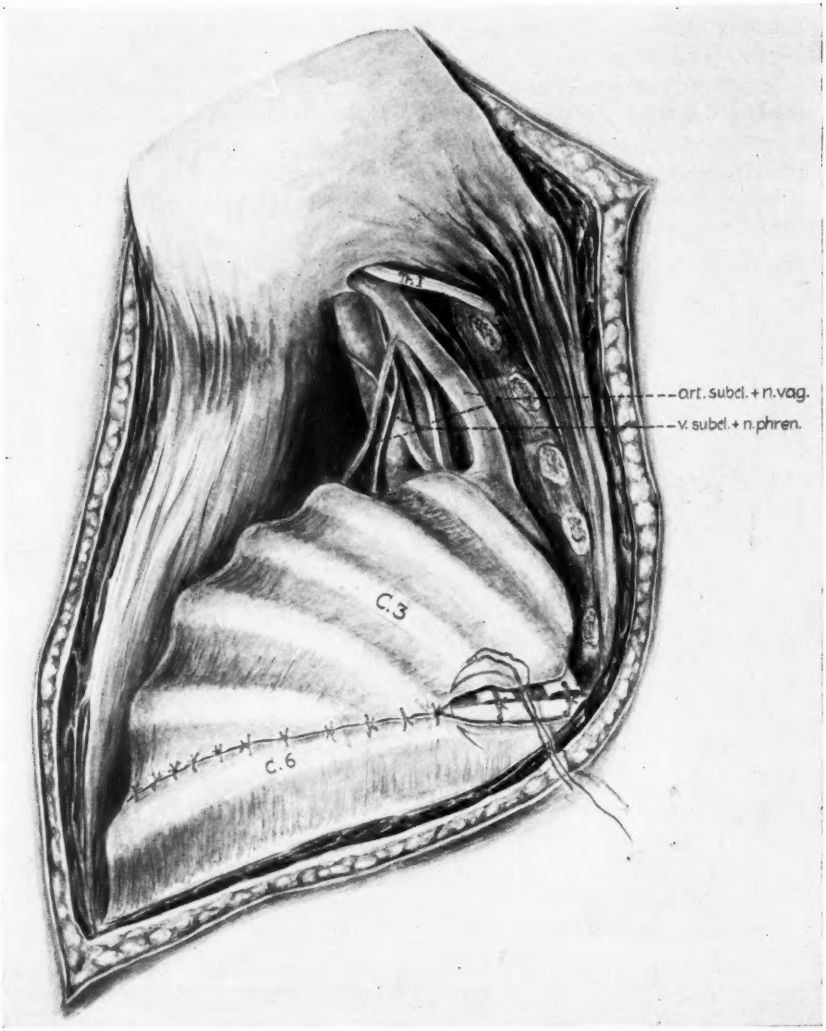


Fig. 7.—The ribs are bent in the cartilages. The sutures are drawn taut and tied when a stable roof of the chest is obtained. The apicolysis has been carried down to the aortic arch (left-sided thoracoplasty).

Third Step.—The ribs are resected as above, but the first rib is left in place. The periosteum is then stripped off its inside for its entire length.

Fourth Step.—The intercostal bundles are divided posteriorly. The extrapleural apicolysis is carried down to the hilum.

Fifth Step.—Fixation is accomplished as above. Special care is taken to resect enough of the second rib in order to make it as straight as possible

(Fig. 3). The second rib is fixed as close to the mediastinum as possible by a stainless steel suture through a drill hole in the sixth rib medial to the tip of the tranverse process. Before the steel sutures are tied a row of interrupted catgut sutures will approximate the two lower intercostal muscle bundles posteriorly into a cushion of muscles between the ribs and the lung (Fig. 9).

Then a fixation of the mediastinal pleura is made in the following manner: A piece of pleura close to the azygos vein on the right side and the aorta on the left side is elevated by a pair of forceps and ligated. One end of the thread used for ligation is threaded on a needle, which is passed through the periosteum of the first rib and the first intercostal bundle and then tied to the free end (Fig. 8). A series of four to six sutures of this type will prevent expansion of the lung even if the pleura is thin, provided the second rib is cut short and placed very close to the mediastinum.

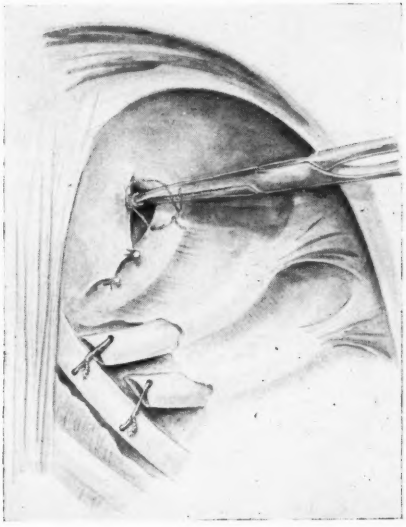


Fig. 8.

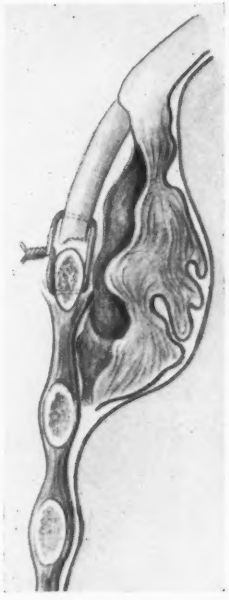


Fig. 9.

Fig. 8.—Fixation of the mediastinal pleura. A piece of pleura close to the azygos vein on the right side and the aorta on the left side is elevated by a pair of forceps and ligated. On one end of the thread used for ligation is a needle, which is passed through muscles left on the first rib and then tied to the free end. Three to six such sutures will prevent expansion of the lung.

Fig. 9.—A row of interrupted catgut sutures will approximate the two lower intercostal bundles posteriorly. Thus a cushion of intercostal bundles is formed between the lung and the approximated ends of the ribs.

After an extrapleural resection naturally no apicolysis can be performed as there is no mediastinal pleura left. Instead the azygos vein on the right side and remnants of the pleura over the aortic arch on the left are fixed to the first intercostal muscle bundle to complete the roof. A careful fixation to the mediastinum will prevent re-expansion even in case some of the stainless steel sutures break.

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Two drainage tubes are inserted intrapleurally and one in the apicolysis space for continuous suction during forty-eight to seventy-two hours.

THORACOPLASTY AS A PROCEDURE PER SE

Results.—The new type of thoracoplasty has been performed as a procedure per se or preliminary to a resection in 18 cases. In 14 cases a five-rib thoracoplasty and in 4 cases a six-rib thoracoplasty were performed. The first rib was always divided both anteriorly and posteriorly and left on the lung fixed as close to the mediastinum as possible.

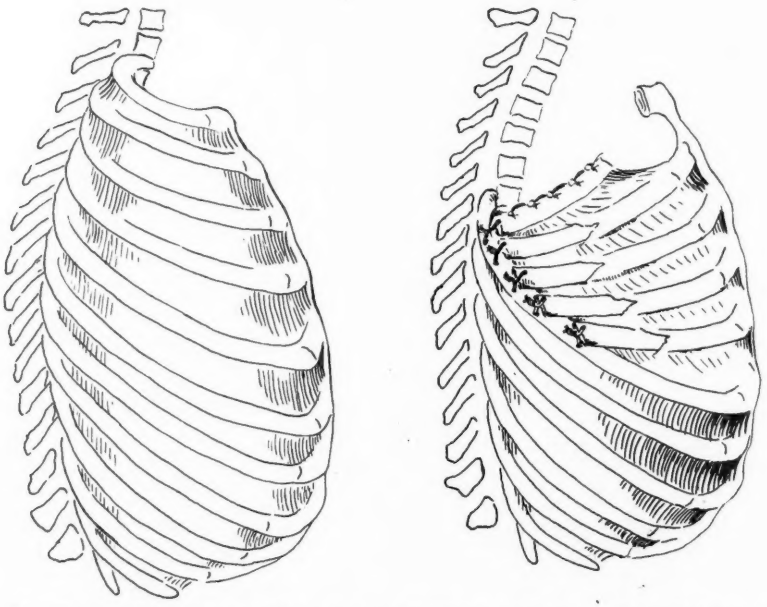


Fig. 10.—The ribs that were parallel have been brought to converge on the posterior part of the sixth rib.

The immediate postoperative course has been smooth in all cases. There has been infection of the apicolysis space in one case. There was no case with atelectasis. The cosmetic result has been good and there are no limitations in the movements of the scapula. As the divided ribs are fixed to the posterior part of the uppermost intact rib, a rounded roof of the chest is obtained and there is no possibility of the scapula's being fastened behind a rib or jumping over a rib. In none of these cases has the lung expanded above the newly formed roof.

Indication.—This type of thoracoplasty is advised in cases with a reasonable chance of cure by this procedure alone. If considerable disease is localized to the anterior segment of the upper lobe, this operation is not performed with resection.

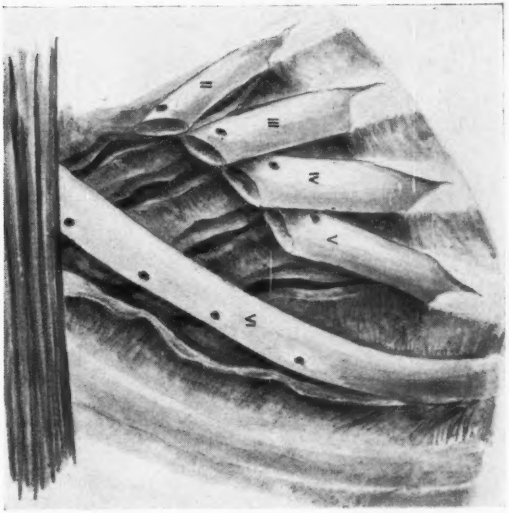


Fig. 11.—A comparatively longer portion of ribs 2 to 5 are resected. The remaining anterior portion of these ribs are freed for some distance on their internal aspects subperiosteally to obtain concentric relaxation.

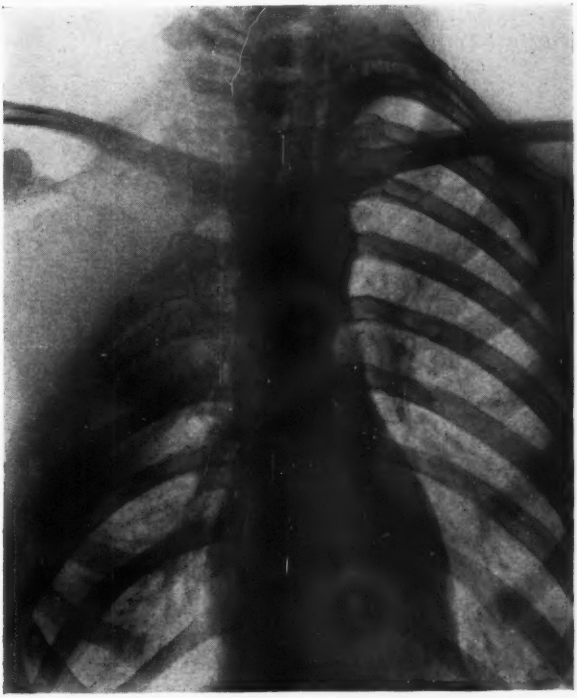
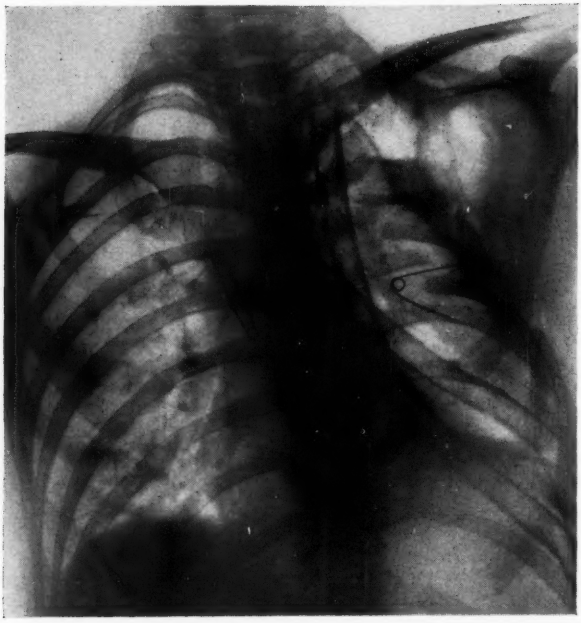
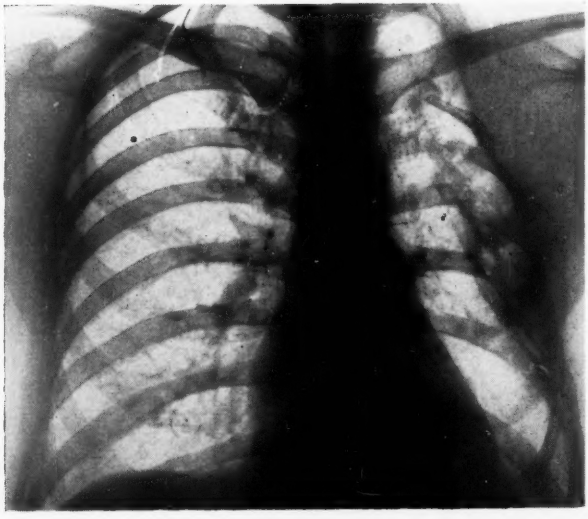


Fig. 12.—X-ray two weeks after a six-rib thoracoplasty on a 22-year-old man. Resection of the posterior ends of ribs 1 to 6 in increasing length. The first rib was fixed to the sixth transverse process. Ribs 2 to 6 were fixed to the seventh rib. The apicolysis was carried down to the azygos vein.



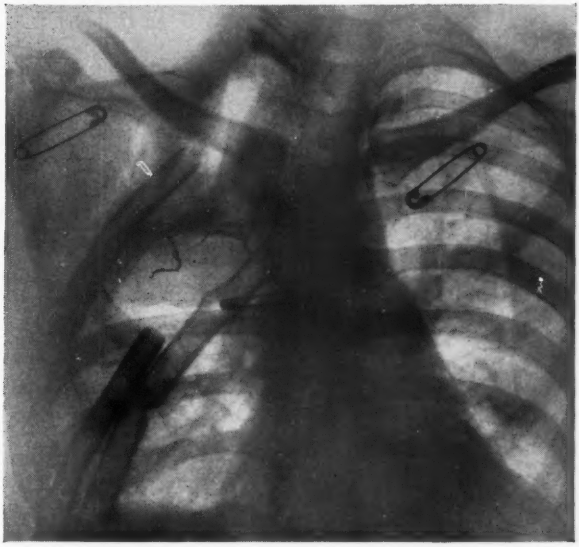
A.



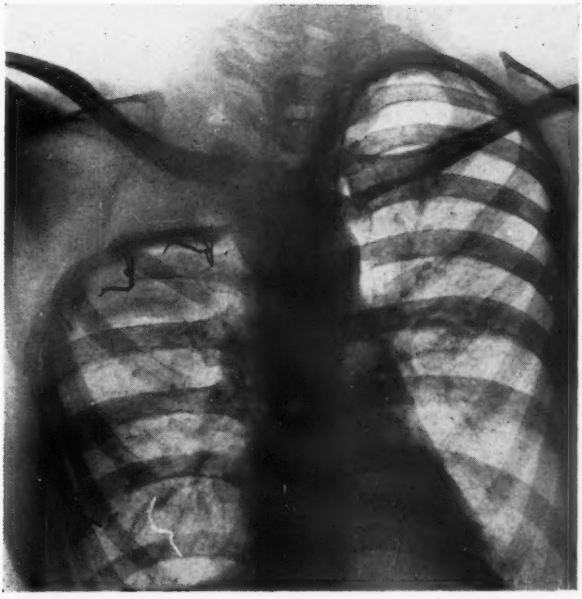
B.

Fig. 13.—*A*, X-ray demonstrating three technical errors in a 32-year-old woman, who had a left lower lobectomy and a simultaneous thoracoplasty. Posterior segments of ribs 2 to 7 were resected. Second and third ribs were fixed to the transverse process of fifth and sixth thoracic vertebra. The remaining ribs were fixed to the eighth with heavy silk through drill holes. (1.) ***Apicolysis was not carried down.*** (2.) ***No fixation of apical pleura was performed.*** (3.) *Too short a piece of the second rib was removed.* Note one drainage tube and the apex of the lung is high above the second rib on this roentgen film taken immediately after operation.

B, X-ray of the same case four months later. The apex of the left lung is above the second rib.



A.



B.

Fig. 14.—*A*, X-ray immediately after right upper lobectomy and simultaneous thoracoplasty in a 27-year-old woman. Resection of posterior parts of the five upper ribs. The apicolysis was carried down to the azygos vein. The first rib was also divided anteriorly. **Ribs 1 to 5 were fixed to the sixth rib with stainless steel sutures through drill holes. Fixation** was performed of the apical pleura.

B and *C*, X-rays of the same patient one month after the operation.

Discussion.—I believe as much concentric relaxation of the diseased area as needed can be obtained by the new procedure. The ribs that were parallel have been brought to converge on the posterior part of the sixth rib (Fig. 10). If comparatively longer portions of ribs 3, 4, and 5 are resected, and these as well as rib 2 are freed for some distance on their internal aspects subperiosteally, a considerable concentric retraction of the diseased area is permitted (Fig. 11). The first rib should, however, be left in its periosteal bed to prevent mediastinal re-expansion of the lung.

This thoracoplasty is a well-tolerated one-stage procedure with practically no possibility of re-expansion of the apex (Fig. 12). As the ribs are left in their periosteal sheaths anteriorly, an eventually extended rib resection may easily be performed.

This operation was also performed as a preparatory operation for resection. At present, however, resection and thoracoplasty are practically always performed at the same operation.

Fig. 14*C*.—(For legend, see page 205.)

THORACOPLASTY IN COMBINATION WITH RESECTION

Results.—The new type of thoracoplasty has been performed in 100 cases in combination with resection. There was one postoperative death.

In 20 cases the first rib has been divided anteriorly, resected posteriorly, and fixed as close to the mediastinum as possible. It is advisable to follow this technique in cases where an extrapleural resection has been performed, and there is danger of infection of the apicolysis space, and when it is felt important to prevent even slight re-expansion of the lung.

A.

B.

Fig. 15.—*A*, X-ray immediately after resection of right middle and lower lobes with simultaneous thoracoplasty in a 22-year-old man. First rib is left intact. Resection of posterior parts of ribs 2 to 6. The second rib was fixed to the sixth transverse process, and ribs 3 to 6 were fixed to rib 7 with stainless steel sutures through drill holes. Apicolysis to the azygos vein. Fixation of the apical pleura. The remaining upper lobe is dislocated down to the diaphragm.

B, X-ray of the same patient two months after the operation.

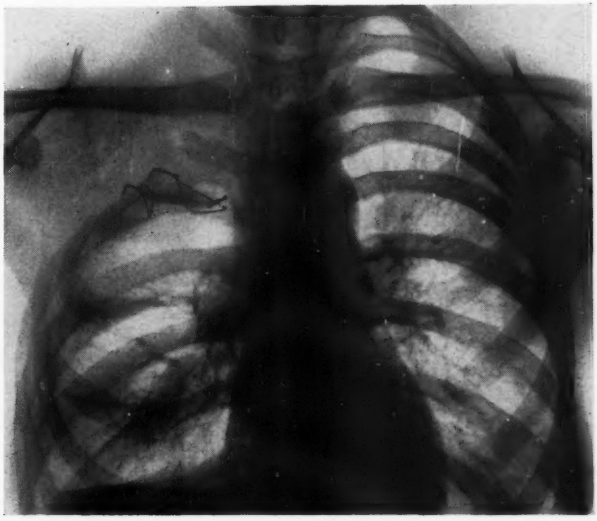
A.

B.

Fig. 16.—*A*, This 38-year-old man had had an eight-rib thoracoplasty on the left side performed five years before. Before the resection the maximal breathing capacity was 46 liters per minute. Bronchospirometry showed 44 per cent of the oxygen uptake and 53 per cent of the minute ventilation on the right side. X-ray immediately after resection of right upper lobe plus superior segment of right lower lobe with simultaneous thoracoplasty. The first rib was left intact. Resection of posterior segment of ribs 2 to 5 which were fixed to the sixth rib with stainless steel sutures. The apicolysis was carried down to the azygos vein. Fixation was performed of the apical pleura. The patient tolerated the procedure well.

B, X-ray of the same patient two months after the operation.

In 80 cases the first rib has been left in place. This modification is somewhat easier and less time-consuming to perform and is used in cases where after resection some expansion of the lung above the new thoracic dome is of no importance. If too short a piece of the second rib is resected, there will be too large a space inside the curvature of the second rib with a re-expansion of the lung (Figs. 3 and 13). If, however, a longer piece is resected from the second rib, making it as straight as possible, it can be fixed close to the mediastinum. If then a careful fixation (Fig. 8) of the mediastinal pleura to the first intercostal muscle bundle is performed, the lung will be kept below the new roof (Figs. 14, 15, and 16). These technical details have been found most important for a good result. In one case in which a giant cavity was opened during the resection, a tuberculous infection occurred in the apicolysis space. This seems now to have been brought under control by conservative means. The cosmetic and functional result has been good (Fig. 17).



A.

Fig. 17.—*A*, X-ray of an 18-year-old woman one month after right upper lobectomy and simultaneous thoracoplasty. The first rib was divided anteriorly and posteriorly. Posterior segments of the five upper ribs were resected. The apicolysis was carried down to the azygos vein. The ribs were fixed to the sixth ribs with stainless steel sutures and nylon sutures through drill holes. Raphe of the apical pleura was performed. Five months after operation bronchospirometry showed 42 per cent of the oxygen uptake and 60 per cent of the ventilation on the right side.

Indication.—This type of thoracoplasty is now always used after resection of at least one lobe. If two segments are removed and small nodules are palpated elsewhere in the lung, a small roof-thoracoplasty is also added for the following reasons:

1. Reactivation of disease has been observed in overexpanded lungs.

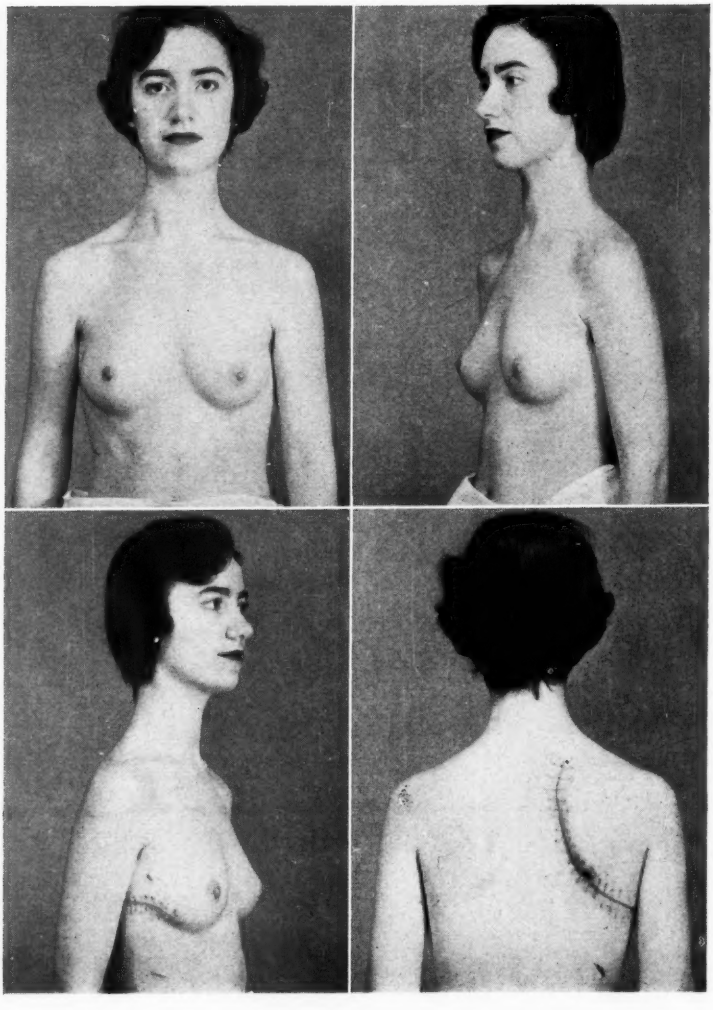


Fig. 17.—*B-E*, The same patient as in Fig. 17, *A*. The cosmetic results have been good. Only a slight enlargement of the groove below the right clavicle can be noticed.

2. If the remaining lung tissue contains several fibrotic areas, it may not completely fill the chest cavity. Any intrapleural air pocket will be potentially dangerous because of infection.

3. A better function of the remaining lung tissue may be obtained. When a thoracoplasty is performed, the percentage of oxygen uptake on the operated side will often keep parallel to the ventilation. On the other hand, a resection without thoracoplasty may result in a comparatively high ventilation and low oxygen uptake on the operated side. Thus the respiratory work on the operated side may be considered uneconomical.

Discussion.—As this type of thoracoplasty will result in a stable roof, paradoxical movements are excluded, cough is more effective, and atelectasis is rarely encountered.

Function studies including arterial oxygen determination during the immediate postoperative period are in progress.

The size of the thoracoplasty may be varied as found necessary. In young patients the costal cartilages are more easily bent but the operation has been performed in several patients over 50 years of age, the oldest being 60 years old.

Summary.—A new technique for thoracoplasty is described and has been performed in 118 patients. There was only one postoperative death. This new thoracoplasty includes: (1) resection of posterior parts of the ribs; (2) apicolysis to the hilum; (3) fixation of the ribs to the posterior part of rib 6 by stainless steel sutures through drill holes. When the sutures are tied, the costal cartilages are bent and a stable roof is obtained.

With the new thoracoplasty paradoxical movements are excluded and the cough is more effective. When used as a procedure per se as much as a seven-rib thoracoplasty is well tolerated in one stage.

The combination of resection with this type of thoracoplasty is a well tolerated procedure.

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LIPOID PNEUMONIA SIMULATING TUMOR

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LIPOID pneumonia is a chronic disease of the lungs caused by the ingestion of oil into the alveolar spaces. It was first recognized by Laughlen[1] in 1925. He reported the autopsy findings in three children who had received oily medications over a long period. Since his report, a large number of cases have appeared in the literature in adults as well as in children.[2-7] Lipoid pneumonia is commonly encountered in the aged, who use mineral oil to alleviate constipation. In the younger age group, oil nose drops or sprays are the chief offenders, especially when cocaine has been added to the preparation. In infants the disease has been reported following the aspiration of milk, vitamin oils, and oily nose drops.[3]

Recently, the increasing incidence of lung cancer has been the subject of considerable speculation. Cases proved by tissue biopsy must be accepted, but our experience at Garfield Memorial Hospital leads us to doubt the validity of cases of lung cancer not histologically proved. It is probable that some of the cases of reported lung cancer without biopsy proof are actually lipoid pneumonia. Despite the modern techniques now available, there are times when it is impossible to distinguish preoperatively between two or more diseases of the lung. Such was true of the six patients to be presented in this paper. In the past, small quantities of oil have been found on occasion in the alveoli of the lungs removed because of bronchiectasis or carcinoma, but cases such as these were not included in this series. The cases comprising this report were studied carefully and no pathologic alterations were found except those resulting from the voluntary ingestion of oil. A bronchogram was not made on three of the patients, and in two instances iodized oil did not enter the segment of lung involved because of occluded bronchi. The large amounts of oil found in the lungs of these six patients could only be accounted for by the voluntary ingestion of oil. Because of the clinical similarity between lipoid pneumonia and tumor, the following cases are presented.

CASE 1.—M. W., a 65-year-old white woman, consulted her physician on June 12, 1942, because she was not feeling well. A roentgenogram of her chest showed a discrete rounded area in the right mid-lung (Fig. 1). When she was admitted to the hospital July 17, 1942, she had no symptoms referable to her chest, and her physical examination was

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essentially negative. Bronchoscopic examination revealed a grayish mass almost blocking the posterior division of the right lower lobe. No bronchogram was made. The preoperative diagnosis was bronchogenic carcinoma. On July 27, 1942, her right lung was removed without complication. The lung weighed 350 grams and its surface was smooth and mottled, dark-red and black. Cut sections showed a 4 cm. firm mass in the lower lobe with surrounding induration. The tissue comprising the mass was gray with flecks of light yellow. There was atelectasis peripheral to the mass. The bronchi were patent except in the involved area. Microscopic examination of sections taken from the central portion of the tumor showed thick, partially hyalinized fibrous bands separating the alveoli. Lymphocytes and plasma cells were diffusely scattered throughout the fibrous tissue and there were occasional large aggregates of lymphocytes. The few residual flattened cells containing hyperchromatic nuclei attached to the walls of circular cavities identified them as alveoli. In addition to the small droplets of oil identified by the use of fat stains, there were large globules of oil present in the thick alveolar walls. Her

Fig. 1.

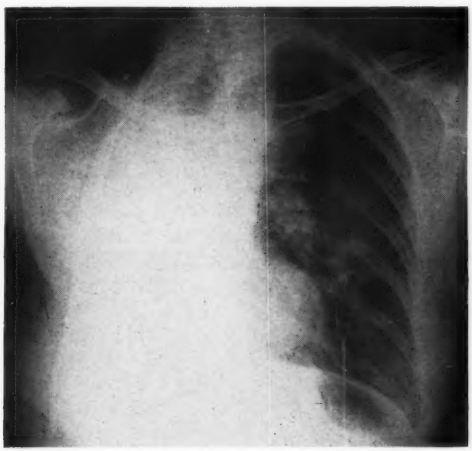


Fig. 2.

Fig. 1.—Roentgenogram in Case 1 showing solitary mass in right mid-lung field.

Fig. 2.—Roentgenogram in Case 1 taken seven years after right pneumonectomy, showing the appearance of lipoid pneumonia in the left lung.

recovery was complete and she moved to a distant location. A communication with the patient seven years later found her in good health. She had not been informed of the diagnosis of lipoid pneumonia and had continued the long practice of taking mineral oil for constipation. Roentgenograms of her chest in 1949 (Fig. 2) revealed a mass similar to that present in 1942. She was advised to stop the use of mineral oil.

CASE 2.—W. G., a 46-year-old white man, became acutely ill in November, 1948, with malaise, generalized muscular pains, and cough. His symptoms persisted, and a roentgenogram of the chest on Dec. 28, 1948 (Fig. 3), showed a localized area of increased density in the right upper lobe. A follow-up x-ray of the chest on Feb. 1, 1949 (Fig. 4), showed the density in the right upper lobe to be a mass which had become larger and more discrete. The clinical and x-ray findings were those of a neoplasm of the right upper lobe, probably bronchogenic carcinoma. A lobectomy subsequently was performed and the pathologic diagnosis was lipoid pneumonia. Additional history revealed that the patient was a high-altitude flyer who routinely used petroleum jelly about his mask. There was no other history of oil. The patient is alive and well at this time.

CASE 3.—F. S., a white man aged 53 years, was admitted to Garfield Memorial Hospital on Aug. 13, 1950, complaining of having had a cold for four weeks. This had been accompanied by fever and increasing fatigue. He had a chronic nonproductive cough and

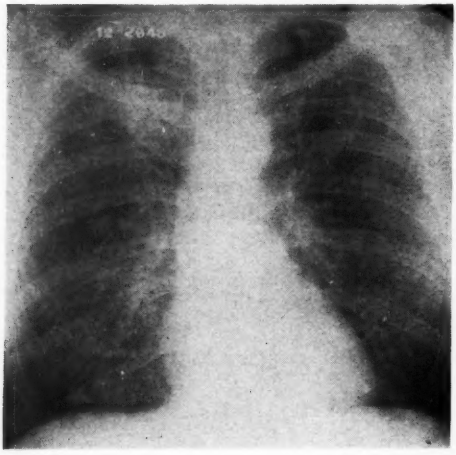


Fig. 3.

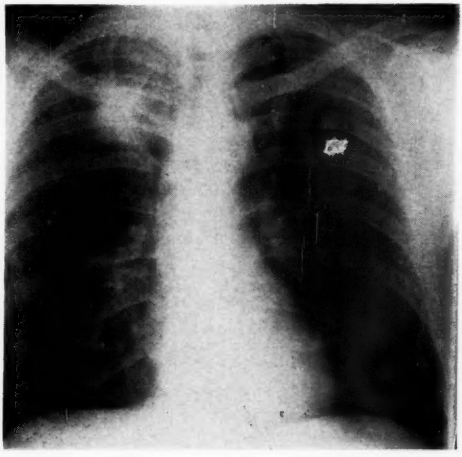


Fig. 4.

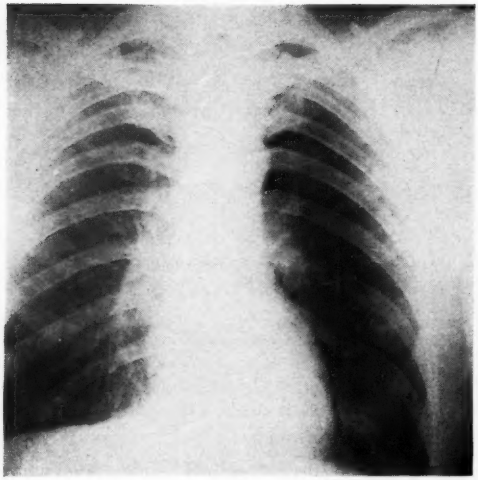


Fig. 5.

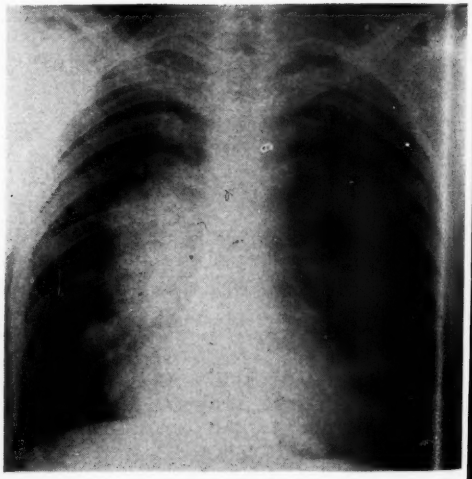


Fig. 6.

Fig. 3.—Roentgenogram in Case 2 showing a localized area of increased density in the right upper lobe.

Fig. 4.—Roentgenogram in Case 2 taken thirty-four days after the original roentgenogram in Fig. 3. Note the density in the right upper lobe which has become larger, more discrete, and appears airless.

Fig. 5.—Roentgenogram in Case 3 showing a normal-appearing chest.

Fig. 6.—Roentgenogram in Case 3 taken ten months after the roentgenogram shown in Fig. 5. Note the large solid-appearing mass in the right lung.

had been treated for pneumonia twice in the past five years. A roentgenogram of the chest, Oct. 12, 1949, appeared normal (Fig. 5). Physical examination was essentially negative

except for dullness to percussion and numerous fine moist râles in the lower right lung field. Laboratory findings were within normal limits. Bronchoscopic examination showed no abnormality except for some rigidity in the right lower lobe bronchus. Cytology and cultures for tuberculosis were negative. Examination of the chest on Aug. 14, 1950 (Fig. 6), demonstrated a lobulated mass extending from the right sixth to twelfth rib posteriorly. Fluoroscopy showed the mass to be fixed. A bronchogram showed normal filling of the bronchi. The impression was lymphoma with extension into the right lung or an unusual-appearing carcinoma in the right lower lobe. At operation on Aug. 17, 1950, the right lower lobe was uniformly firm. The entire lung was densely adherent to the chest and the diaphragm and hilar nodes were greatly enlarged. A frozen section diagnosis was equivocal but was thought to be fibrosarcoma. A pneumonectomy was accomplished with difficulty because of many adhesions. The lung weighed 1,000 grams. The entire surface was covered by fibrous tags. It was partially collapsed and bluish-red in the upper lobe, but was solid and grayish-brown over the lower lobe and inferior portion of the middle lobe. The interlobar fissures were indistinguishable. Cut section showed homogeneous, spongy, yellowish-gray tissue throughout all the lower lobe and approximately half the middle lobe. The bronchi were slightly reduced in diameter but were patent throughout. Microscopic sections of the lower and middle lobes showed alveoli devoid of lining cells and surrounded by wide bands of fibrous tissue. The alveoli contained large masses composed of desquamated alveolar lining cells, debris, and lipophages. Sections stained with Sudan III showed small particles of fat in the fibrous stroma and large quantities of fat in the alveoli. The patient died following the operation. Autopsy showed small amounts of fat present in the left lung, and some of the alveolar lining cells were enlarged, but there was no increase in the amount of fibrous tissue in the alveolar walls. After the death of the patient it was learned that he had taken mineral oil as a laxative for ten years. It was ascertained that he took a large draft of mineral oil before retiring every night and also upon rising in the morning.

CASE 4.—J. R., a 60-year-old white man, was admitted to the hospital on Sept. 17, 1932, following a routine physical examination which revealed a lesion in his right lung. The patient complained of slight dyspnea, but he had no cough or pain. The physical examination was essentially negative and the results of routine laboratory tests were within normal limits. Roentgenograms of the chest on Nov. 16, 1951, had demonstrated an irregular 7 by 14 cm. density with a nodular border in the right middle lobe which had remained unchanged in appearance since Aug. 12, 1951. The major fissure was slightly elevated due to fibrosis or collapse of the middle lobe. A bronchogram showed failure of the medial portion of the middle lobe to fill. Tomographic study of the middle lobe demonstrated the bronchi to be filled with air and surrounded by a homogeneous density, having the appearance of segmental fibrosis. The lesion was believed to be either inflammatory or neoplastic. A bronchoscopic examination revealed no abnormality. Cytology was negative and cultures for tuberculosis showed no growth. On Sept. 17, 1952, the right middle and lower lobes were resected without difficulty and the patient made an uneventful recovery. Grossly, the inferior segment of the middle lobe was firm, slightly nodular, and mottled yellowish-gray. The anterior division of the lower lobe presented a similar appearance. Both lobes showed decreased crepitation in the involved areas. Cut sections showed fairly well demarcated areas of firm yellowish-gray tissue which cut with increased resistance. Microscopically, the alveolar walls were markedly thickened due to fibrous tissue, lymphocytes, and numerous fat droplets. Most of the alveoli contained partially phagocytosed oil, debris, and numerous conglomerate giant cells. In some areas small segments of alveolar lining cells remained attached to the alveolar wall. These appeared to have fused into a syncytium with elongated pyknotic nuclei and purple, finely granular cytoplasm. After the patient recovered, he readily admitted having taken mineral oil for at least three years for the relief of constipation. The patient is now living and well.

CASE 5.—T. J., a 56-year-old white man, was admitted to Garfield Memorial Hospital on Aug. 27, 1953. A mass was found in the right lower lobe on a routine chest x-ray.

His history revealed increasing fatigue and a chronic productive cough for four years. Hemoptysis had occurred four times during the past six months and he had experienced vague epigastric distress periodically. He admitted having used oily nose drops regularly for over four years. The physical examination was essentially negative except for râles over the right lower lobe. Laboratory examinations were not helpful. Bronchoscopic examination revealed thickening and edema of the bronchi leading to the right lower lobe. The cytology and cultures for tuberculosis were negative. Roentgenogram of the chest on Aug. 28, 1953, showed a soft tissue density measuring approximately 5 cm. in diameter located in the posterior portion of the right lower lobe. A bronchogram showed filling of all the major bronchi except those in the region of the mass. The preoperative diagnosis was either lipoid pneumonia or tumor. At operation on Sept. 14, 1953, a mass was palpated in the right lower lobe and the adjacent part of the middle lobe. A frozen section diagnosis of lipoid pneumonia was made, and the middle and lower lobes were removed. Grossly, the lobes weighed 311 grams and were partially crepitant. Cut sections showed a 3 by 2.5 cm. poorly circumscribed, firm, light yellowish-gray mass in the basal portion of the lower lobe. In the bronchus leading to the diseased tissue in the lower lobe was an irregular 0.8 cm. concretion. Microscopically, the lesion consisted of masses of edematous fibrous tissue interspersed with partially collapsed alveoli. Deep in the fibrous masses were groups of fat-filled phagocytes, lymphocytes, and a few plasma cells. The alveoli contained a few lipophages and were partially lined by cuboidal cells. Some of the alveolar lining cells remained attached to the wall while others formed conglomerate masses in the alveoli.

CASE 6.—W. W., a 51-year-old white man, was admitted to Garfield Memorial Hospital on Feb. 5, 1953, complaining of a cold which had not responded to antibiotic therapy. He had had pain in the right chest and a severe cough for two months. Physical examination was negative except for a few moist râles in the right hilar area. Laboratory findings were within normal limits. Bronchoscopy revealed diffusely inflamed mucosa on the right side. Washings showed some suspicious cells and were negative for tuberculosis on culture. A bronchogram was not done. A roentgenogram of the chest showed enlargement of the right lung root. The appearance of the shadow was such that the possibility of a bronchogenic carcinoma must be considered. A right pneumonectomy was done on Feb. 6, 1953. There were many pleural adhesions, and the hilar lymph nodes were enlarged. The lung weighed 375 grams and was crepitant except for a centrally placed 5 cm. mass in the right lower lobe. Cut section showed an ill-defined area of induration, measuring 4 cm. in diameter, with a small central cavity containing oily material. The wall of the cavity was ragged and about it was a thick layer of grayish-yellow, firm, finely granular tissue. Histologically, the alveoli were irregular in shape because of the thickened fibrotic alveolar walls. The alveoli contained a large number of lipophages and were lined by low cuboidal cells with prominent nuclei. The alveolar walls contained many fat-filled phagocytes, and scattered lymphocytes with a few plasma cells and neutrophils. It was discovered after the operation that the patient had used approximately a pint of mineral oil a month for at least a year for relief of constipation.

While this series of cases is not large, the symptoms and findings are fairly characteristic of a larger group of nonsurgical patients with lipoid pneumonia found at Garfield Memorial Hospital during the past five years. The importance of this preventable disease should not be minimized because it is often disabling. The disease may sometimes be fatal. The autopsy findings on five patients who died of lipoid pneumonia at this hospital were recently reported[8] (including our Case 3).

Only three patients in this series sought medical advice because of their symptoms. The others were referred for investigation because of asympto-

matic lung lesions found on routine roentgenographic examination. Most of the patients had rather vague indefinite complaints and no single complaint was common to all patients. On questioning, four had a chronic cough and two had slight pain in the chest. One patient had repeated hemoptyses and one was slightly dyspneic.

The diagnosis of lipoid pneumonia cannot be made on the basis of clinical findings alone. Physical signs are not specific and vary with the size, position, and character of the lesion. Clinical laboratory tests are equally unrewarding and serve only to rule out certain other diseases. It has been determined in a large series of cases[2] that lipoid pneumonia occurs predominantly in the right lung. This is presumably due to the anatomic differences between the two lungs. The right lung was involved in every patient in this series. It has also been determined that the right lower and middle lobes are most frequently involved. This was the case in this series, the right upper lobe being involved in only one instance. Only one of the patients in this group of six was a woman, although in larger series the sexes were almost equally divided. The ages of our patients ranged from 46 to 65 years.

In all but one case the history of oil ingestion was obtained after the oil had been found in the resected lung. According to the histories, the disease was caused by mineral oil taken for the relief of constipation in four cases, and by nose drops and petrolatum each in one instance.

A pneumonectomy was performed on three of the six patients because of extensive involvement of the disease in one case and the medial location of the tumor in the other two cases. The right middle and lower lobes were removed in two cases because of extensive disease, and the right upper lobe only was removed in the patient who had localized tumor. In four patients rather extensive pleural adhesions were present which were usually unrelated to the site of the disease. Lysis of adhesions slowed the operating time because of their great vascularity. The hilar and mediastinal lymph nodes were greatly enlarged in two instances. Histologically, these nodes were hyperplastic and the hilar nodes in Case 3 contained oil. All the pulmonary lesions were described at the time of operation as being firm and rubbery, and in one case there was dimpling of the pleura over the mass. Lipoid pneumonia was not recognized in any of the cases at the operating table because of its close similarity to carcinoma. Lipoid pneumonia was suspected in several cases and frozen sections were requested. The frozen section diagnoses were incorrect in some of the early cases, but later lipoid pneumonia was suspected from the yellowish-gray appearance of the cut section of the lung. In these cases fat stains were quickly made which confirmed the diagnosis. One patient died following the operation from hemorrhage into the pleural cavity. The others recovered without complications and are living at the time of this report. The woman described in Case 1 was not informed of the nature of her disease after her right pneumonectomy. She moved, subsequently, and was not contacted by us for seven years. At that time it was ascertained that she had been constipated for many years and had routinely

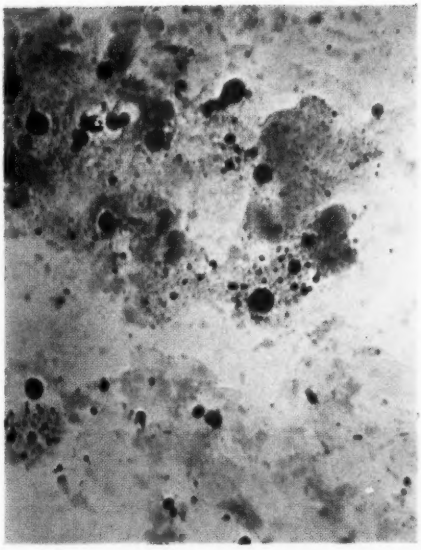
taken mineral oil for relief. The roentgenogram taken seven years after pneumonectomy showed an area of density in the left lung field similar to that seen on the right three years before.

In general, the roentgen features are those of fibrosis and consolidation. The disease is usually multilobular and may remain unchanged for years. The fibrosis consists of fine linear and small nodular densities which may or may not reduce the size of the lobe. The appearance is that of spun glass, and it may extend to the pleural surface; however, pleural effusions are rare. By means of Bucky film and a fine focus tube an area of apparent consolidation can be shown to contain air and present the spun-glass appearance. This finding is of great importance in diagnosis, for it rules out a solid tumor or complete collapse. The lower lobes, particularly the right, are the usual sites of the disease, but the axillary portions of the upper lobes may also be involved. The disease may affect an entire lobe and produce an airless appearance; for example, involvement of two middle lobes has been seen, one occurring coincidental with sarcoid and another in a patient without other pathology. One case showed complete collapse of the middle lobe and the bronchi could not be identified grossly. Lipoid pneumonia may simulate atypical pneumonia, lobar pneumonia, tuberculosis, neoplasm, infarction, metastatic lesions, or bronchiectasis. In every case in this group there was either apparent bronchial occlusion or a nodular mass resembling tumor.

The diagnosis of lipoid pneumonia is made on routine hematoxylin-and-eosin-stained tissue, though fat stains are always used for confirmatory purposes. This diagnosis is not made when the sudanophilic material is found only in the alveoli and alveolar walls, for this is usually due to preoperative iodized oil studies. When sudanophilic material is found in the fibrous tissue some distance from the adjacent alveoli, it is considered to be ingested oil. Control lungs subjected to iodized oil studies preoperatively have not shown penetration of oily substances beyond the alveolar walls. It is known that varying amounts of intra-alveolar oil are removed by physiologic and mechanical means. Intracellular oil was found in the sputum of one patient for a month after the introduction of iodized oil into the lungs for diagnostic purposes. Between August, 1950, and November, 1953, a period of three years and three months, fifty-seven patients were operated upon at Garfield Memorial Hospital for primary carcinoma of the lung. During the same period three patients were operated upon for lesions which ultimately were proved to be lipoid pneumonia. Though these figures are too small to be of statistical significance, they indicate the difficulty in establishing a correct preoperative diagnosis. The figures also suggest that lipoid pneumonia is a relatively common condition.

A strong index of suspicion is the best aid to the diagnosis of lipoid pneumonia. This is shown by the relatively large number of such cases found at Garfield Memorial Hospital in recent years. It is important to make a diagnosis in suspicious cases before undertaking a major operative procedure, for surgery is probably not the treatment of choice in all cases. A diagnosis of lipoid pneumonia may be made on the basis of a satisfactory history of the

Fig. 7.



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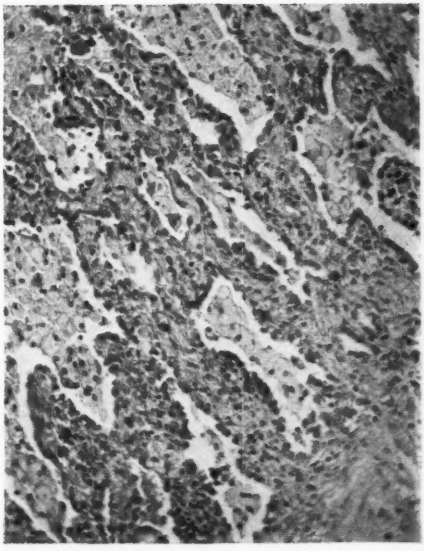

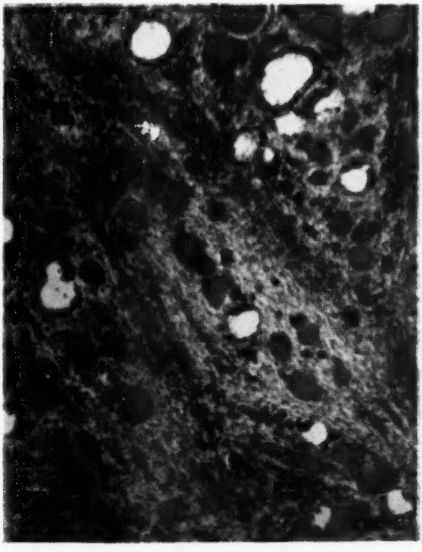

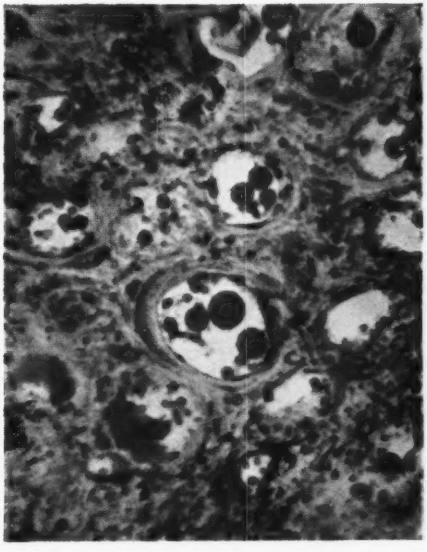

Fig. 9.

Fig. 10.

Fig. 7.—Fat stain on sputum from Case 5 showing sudanophilic material within phagocytes. (Sudan III, ×320; reduced ⅙.)

Fig. 8.—The lung in Case 3 showing the thickened alveolar walls separating alveoli lined by cuboidal epithelium and filled with lipophages. (Hematoxylin and eosin, ×165; reduced 2/11.)

Fig. 9.—Fat stain of lung from Case 1 showing marked fibrosis and entrapped oil. The alveoli are reduced in size and are functionless. (Sudan III, ×100; reduced ⅙.)

Fig. 10.—Fat stain of the lung in Case 4 showing the end result of lipoid pneumonia. (Sudan III, ×110.)

ingestion of oil, consistent roentgen findings, and the finding of oil within phagocytes in the patient's sputum. The technique for collecting specimens of sputum for examination is important. The patient's sputum must be from the bronchi and should be collected in a clean glass container prior to eating breakfast. Smears stained with Sudan III are positive when particles of sudanophilic material are present within the phagocytes. Extracellular fat is of no significance.

Most patients who use oily medications apparently have no need for active treatment. Patients who develop dyspnea or shortness of breath should be treated symptomatically and advised to stop medication. Surgery is indicated for any patient who gives a history of ingestion of oil, whose sputum contains oil and in whom a pulmonary lesion cannot be differentiated roentgenologically from a tumor. The best treatment is prevention.

We wish to express our appreciation to Dr. Roy G. Klepser for permission to include Case 6 and to the Armed Forces Institute of Pathology for Case 2.

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Announcements

THE AMERICAN ASSOCIATION FOR THORACIC SURGERY

Notice of Annual Meeting

The Thirty-fifth Annual Meeting of the American Association for Thoracic Surgery will be held April 24, 25, and 26, 1955, in Atlantic City, New Jersey. Headquarters will be at the Chalfonte-Haddon Hall.

Requests for Hotel Reservations

These should be mailed directly to Miss Doris Sears, Convention Manager, Chalfonte-Haddon Hall, Atlantic City, New Jersey. Please mention this Association, the type of accommodation desired, date and approximate hour of arrival. If accommodations are desired elsewhere in Atlantic City, please communicate directly with the hotel of your choice.

Thoracic Surgical Forum

By vote of the membership, the Forum is to be continued for the presentation of short papers on current thoracic research, experimental problems, anatomical studies and modified or new surgical techniques. The inclusion of any considerable amount of clinical material in these reports makes the choice more difficult and the Program Committee reserves the right to reject such papers or to suggest their transferral to the regular program. Papers at this session will be limited sharply to ten minutes, including the showing of lantern slides or other illustrative material. At the discretion of the President, three minutes may be allowed as the maximum discussion for each paper.

These papers will be published together in one issue in the JOURNAL OF THORACIC SURGERY. Maximum length: 3,000 words without illustrations. If illustrated, an appropriate number of words must be subtracted for each cut used.

Abstracts for Papers

Abstracts for the presentation of papers at the 1955 meeting, including papers before the Forum, must be received on or before Dec. 15, 1954; otherwise they will not be considered by the Program Committee.

Abstracts should be labeled "For Thoracic Surgical Forum," or "For Regular Program."

Five, repeat, five copies of each abstract must be sent to the Secretary of the Association, Dr. Paul C. Samson, 3959 Happy Valley Road, Lafayette, California. They should not be sent to the Editor.

The abstracts should contain from 200 to 250 words and accurately reflect the contents of the completed paper.

Applications for Membership

Applications for Associate Membership in the Association must be received by the Membership Committee not later than Dec. 15, 1954; otherwise, the applications will be deferred for consideration until 1956.

Applicants must be sponsored by three Active or Senior members of the Association. In addition to the signatures on the application form, the sponsors must forward a *separate* letter concerning the applicant directly to Dr. Lyman A. Brewer, III, Chairman of the Membership Committee, 2010 Wilshire Blvd., Los Angeles 5, Calif.

Completed application forms and the sponsoring letters *independently* sent by the three sponsors must be received by Dr. Brewer not later than Dec. 15, 1954, to be considered for action in Atlantic City.

Sponsors are reminded that *new* letters of recommendation must be forwarded to the Membership Committee should their applicants be held over for reconsideration a second year.